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Laboratory Practice
of ORGANIC CHEMISTRY

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of Organic Chemistry

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Preface

The main feature of this volume is an unusually extensive, but informal treatment of the principles underlying laboratory manipulations in organic chemistry. Part I consists largely of this theoretical material. Part II includes synthetic experiments and a few examples of elementary qualitative and quantitative analysis. Essential explanations of principles are thus kept distinct from directions for experiments which a given instructor may not wish to use. Cross references are provided, however, in both parts. Enough experiments are included to cover the needs of a year course, with many options for superior students.

A tendency to curtail laboratory work in organic synthesis, recently reported from certain universities, would seem to indicate dissatisfaction with courses that do not go much beyond "cookbook" activities. One leading institution has completely eliminated synthesis from certain life-science curricula. The time thus saved is being devoted to qualitative and quantitative analysis, which in the opinion of the authorities concerned offer greater values in chemical training.

The author feels that this disparagement of organic synthesis really arises, not from any inherent fault in the kind of work, but rather from inadequacy of class discussions of the principles governing such experimentation. Many of these principles may, to be sure, be found in somewhat abstract form in courses of physical chemistry —which many students unfortunately never reach. Although branded as elementary physical chemistry, this theoretical material is after all best illustrated in the organic laboratory. Phase changes and the acid-base relations are particularly good examples. In the author's laboratory, therefore, extra time is scheduled for lecture-discussions and somewhat less for laboratory manipulation. Without apology the author frankly admits that portions of the text are beyond the mental reach of mediocre students; for example, the Du-

claux analysis and the distinction between melting range and melting point.

Comparatively few exercises of the so-called "introductory" type are included. Experiments leading to definite exhibits of preparations or analytical reports are taken by students more seriously than tests that 'end in the scrap jar or sink. Furthermore, they are much more easily administered by a busy instructor with laboratory assistants of varying competence.

In the revised edition, the following new experiments have been added: Fractional distillation, propylene and propylene dibromide, chloroform, bromoform, iodoform, mucic acid, β-d-glucose pentacetate, inversion of sucrose, cellulose nitrate, quinone (bromate method), n-butyl benzene, n-butyl dimethyl carbinol, propionic acid, acetoxime and nitropropane-diol from nitroparaffins, maleic and fumaric acids, Diels-Alder synthesis, phenacetin and sulfanilamide.

Improvements have been made in many experiments; for example, a substantial improvement in yield of n-butyl bromide is obtained from new directions. Extensive additions and rewriting have been carried out in the chapters dealing with theory.

Questions, problems and a number of equations have been included in both parts I and II. Occasionally representations of reactions are left incomplete, particularly where the balancing of an equation is of importance. In directions for preparations frequent use is made of molal and normal instead of simple metric units of quantity, again with the purpose of directing attention to the fundamental basis of calculation.

The author wishes to thank his colleagues in the chemistry department, and particularly Messrs. Wm. G. Young, T. L. Jacobs, T. A. Geissman, S. Winstein, and C. Ernst Redemann for valuable suggestions and assistance in conducting trials of laboratory directions by students. Acknowledgment is also given of assistance by numerous students, both in proposing and testing procedures. Recognition is also given of suggestions from well-known laboratory manuals, especially the valuable works of Adams and Johnson, Adkins and McElvain, L. F. Fieser, Oliver Kamm, and Shriner and Fuson.

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Contents

PART I

THEORY AND GENERAL TECHNIQUE

PART II

LABORATORY EXPERIMENTS

Part I

THEORY *and* GENERAL TECHNIQUE

CHAPTER 1

Introduction

From inorganic chemistry we learn that the mixing of magnesium hydroxide with sulfuric acid is a simple, straightforward experiment. There is little concern about the identity of the final product, or the amount thereof. Presuming that the experiment was based on sound chemical arithmetic, the full amount of magnesium sulfate called for by theory may be expected, even though the technique may have been bad.

From organic chemistry one learns that ethyl hydroxide (ethyl alcohol) also reacts with sulfuric acid. This seems to be a simple analogy, but the problem is no longer a mere matter of formation of water and a salt. Two or more competing reactions are likely to set in. These reactions lead to different products. If the wrong reaction happens to be the most rapid, the student experimenter ends the day's work wistfully wondering why he got a low yield of the product which he originally sought.

Further investigation of the ethyl alcohol-sulfuric acid reaction shows that striking changes in the relative speeds of competing reactions may be made by careful adjustment of temperature, concentration, and other factors. Perhaps the most undesirable reaction may be retarded by dilution, or the useful reaction accelerated to a relatively high degree by simple heating to some controlled temperature.

In other cases a desired reaction may be favored by selection of some special solvent or by addition of a catalyst. The desired product may be an intermediate in a short chain of successive reactions between a reagent and a useless final product. If one can expel this intermediate from the scene as fast as it is produced, and thus before a later reaction can destroy it, failure is turned into success with no real change in chemical principle. In brief, a whole field is opened in which laboratory technique comes to the forefront. Special

devices are called into service, such as the reflux condenser, fractionating column, separatory funnel, Buechner filter, oil bath, Claisen flask, etc.

To apply such technique intelligently one should have an adequate understanding of the fundamental principles underlying manipulation. Such factors as vapor pressure, melting phenomena, and mutual solubility are examples. Accordingly the first part of this volume is devoted to a critical discussion of these principles. Secondly, a list of practical experiments is given to illustrate principles.

In the industrial world the possibility of selective control of chemical reactions is commanding the keenest interest. For example, the new American synthetic process for making glycerol (glycerine) depends essentially on the skillful selection of a certain reaction of chlorine which is used to outrun the expected, but undesired, competing reaction. Such studies occupy the attention of a relatively new class of researchers known as "physical organic chemists."

Not only the chemist, but the physician, horticulturist, cosmetician, lacquer manufacturer, etc., require a great variety of organic compounds and should know the rules governing their complex behavior. For example, a medical blunder once cost the life of a patient because the physician did not know how to neutralize the strongly acidic salt of an organic base before intravenous injection. The organic chemical industry is now supplying a bewildering array of new compounds for both new and old technology—to the painter, textile cleaner, toymaker, auto accessory manufacturer, and a thousand other artisans.

THE SIGNIFICANCE OF
LABORATORY WORKMANSHIP

One of the prime characteristics of the competent worker in organic chemistry is an intelligent appreciation of the motto "SAFETY FIRST." The advent of volatile, highly inflammable solvents into student experience calls for immediate attention to hazards involved.

Anyone is likely to pass caustic comment about the foolish citizen who got into the newspaper by heating gasoline in a kettle on the kitchen stove so as to improve its cleansing powers. Unfortunately

the same critic, working in an organic laboratory, no longer thinks of the term "gasoline," and occasionally boils acetone or ligroin in an open flask over an open Bunsen flame. His motive is the same—to improve the solvent power of the liquid—but the blunder is even less excusable than that of the untrained layman with the gasoline.

The student entering upon this work should at once become familiar with the varying degrees of danger in handling solvents (§ 34), and read the discussion on "Laboratory Accidents" on the inside front cover.

In this course of study the student is normally expected to present to the instructor at the conclusion of each assignment a finished chemical product. It is of foremost importance that the quality of this product be good. Of hardly less significance is the desirability of a good yield. If, however, one is contented with these two achievements alone, he is promptly branded as a mere cookbook operator. No real skill is acquired from such experimentation unless the student knows what he is doing while he is doing it, and why.

In many laboratories the last statement is taken so seriously that a student is not permitted to withdraw necessary supplies from stock, or to start an experiment, until he has demonstrated in an oral or written quiz that he understands what he is about to do. The plan is highly commendable if the instructor can spare the necessary time.

Lastly, it is an open secret that the laboratory instructor in organic chemistry often identifies a good workman by discovering clean apparatus, neatly assembled, on a clean laboratory desk. This does not mean the total absence of all extraneous matter not actually in use. Evidence of slovenly workmanship appears not so much from the presence of a recently used match or a few drops of water splashed during current operations. It is yesterday's or last week's dust, dirt, or disorder which is more characteristic and thus inexcusable.

CHAPTER 2

General Laboratory Requirements

Note. *In view of differences in equipment and arrangements in various laboratories, optional methods are occasionally presented here. Follow only those sections of this chapter specified by your instructor.*

1. Notebooks. Each student keeps a bound notebook of adequate size (about 8 by 10 inches). Loose-leaf books are not admissible. The course calls for a complete record of failures as well as successes, not a polished essay composed after troubles and errors have been cleared away.

Write frankly in the notebook any comments on operations which went wrong. Do not tear out sheets carrying unsatisfactory data; such action merely indicates slovenly habits of writing records. "Writeups" done at home after experiments are completed are discounted.

Plan your written work, as well as laboratory performance, in advance. See that there is proper space for all data, particularly those in tabular form. If the experiment calls for records of weights, volumes, or other numerical results, write these values directly in the notebook, not on scraps of paper.

While it is not necessary to copy extensive directions for experiments, the student should include sufficient descriptive detail so that the whole report is readily intelligible to a chemist. The record should show a critical appreciation of the possible sources of trouble. No one gets a full 100% yield of an entirely pure organic compound from any of these experiments, and the really intelligent student should be able to explain in some degree why reality falls short of the ideal. Any student who feels that the writing of notebooks in the chemical laboratory is merely an academic chore should ask the opinion of the chief chemist of any chemical industry. He may learn something that will surprise him.

When the experiment is complete, the student is expected to write a brief summary of results, separate from the notebook, and to submit this together with any bottled material to the instructor. If the work is accepted, the instructor merely retains this report as a record for his private files. Two forms of such a report are commonly used (§ 2 or § 3).

2. Card Report. A common office filing card, 4-by-6-inch size, may be used. The following is an example.

Experiment No. 2   Howard A. Smith

n-PROPYL BROMIDE

$$C_3H_7OH + KBr + H_2SO_4 \rightarrow C_3H_7Br + KHSO_4 + H_2O$$

Calculation based on 60 g. (60/119 mole) of KBr:

$$\frac{60}{119} \times 123 = 62.0 \text{ g. Theoretical yield}$$

48.5 g. Actual yield

$$\frac{48.5}{62.0} = 78.2\% \text{ Percentage yield}$$

B. pt. (literature) 70.9°   Boiling range of product 70–72°

Further explanation of the above calculation is given in § 29.

Please write number, name, and title in the uniform positions indicated above, for convenience in examination of files.

3. Special Report Form. A special printed blank form may be provided according to notice given by the instructor. Fill out all blanks that are appropriate to the particular experiment at hand.

4. The Finished Chemical Preparation. Unless some special question has been encountered, do not occupy the time and attention of the instructor or assistant with the results until notebook and report are complete and the product has been placed in the proper container for inspection. Learn the routine of the laboratory, in particular knowing the proper place for final storage or disposal of material. Do not throw away any products—they are of value in

the laboratory.   Some command prices in the range of several dollars per pound.

Cloudiness in a liquid preparation usually indicates that the material is not dry.   Such a cloudy liquid may become clear in a few hours by yielding its emulsified water to the surface of the glass container.   This may lead to the false impression that the bottle itself had not been properly dried.   Solids which have not been properly dried betray that fact by clinging to the side walls of the container.

5. Use of Bottles.   If standard bottles are provided for organic preparations, weigh each before introducing the material, recording the so-called "tare weight" on the label.   One may then readily determine the net contents of the container at any future time regardless of partial withdrawal of material.   Labels should be written or printed neatly in ink.   Avoid misplaced, pencil-scrawled labels; write them properly once for all.   The standard of workmanship is merely that required in any first-class pharmacy.   The following is an example of a label:

---

tert-BUTYL CHLORIDE

B. p. 52°
Yield 37.5 g.   Tare 41 g.

JOHN W. WILLIAMS

CLEANING AND DRYING GLASSWARE

6. Use of Solvents.   Of prime importance is the fact that laboratory apparatus is most easily cleaned immediately after use.   Glass is preferentially wetted by water rather than the various oily and tarry constituents accompanying the water on the surface of a newly soiled vessel.   Simple rinsing with water may eliminate the organic matter at this stage.   If through delay the water evaporates, the tar reaches the actual glass surface and adheres tightly.   It is well to develop the habit of washing each piece of apparatus as soon as it is emptied.

Soap and trisodium phosphate may well be used, particularly in glassware accessible to a brush.   If a tarry contamination is known

to be basic in character, as with amines, dilute hydrochloric acid may be effective; if acidic, as with phenolic residues, dilute sodium hydroxide will serve.

Tarry matter is often handled to better advantage with a volatile solvent intermediate in character between water and saturated hydrocarbons. Acetone and benzene are particularly effective against semioxidized tars commonly arising in experiments with the aromatic series of compounds.

7. Use of Abrasive Washing Powder. A high-grade household washing powder, containing an abrasive which will not scratch glass, is convenient and effective on vessels to which access with cloth or brush is possible. Punch only one hole in the top of the sifter can, so that the powder may be directed into a narrow-mouthed vessel without spilling.

If the conventional method of scrubbing a vessel with washing powder and water is inadequate, the powder may instead be moistened with an organic solvent such as acetone. The resulting paste promptly picks up, if not completely dissolves, a refractory tar, and buries it in a mealy mass. The solvent may then evaporate without inconvenience. The addition of a small amount of water disperses the accumulation, leaving only a simple final rinsing operation.

8. Chromic-Sulfuric Acid "Cleaning Solution." For decades organic chemists have placed their principal dependence on a mixture of chromic acid (CrO_3) and concentrated sulfuric acid. Directions for preparation of this material are given in § 181. The cleaning solution has considerable value not only by virtue of its oxidizing capacity, but probably still more because it is a powerful reaction solvent which has the power to convert a great variety of semi-oxidized compounds, including tars, into salts. (See § 170 (7).)

It is customary to keep on hand an ample supply of this cleaning solution, using perhaps the entire quantity in each operation. After the soiled surface of the vessel has been thoroughly wetted with the solution, the main supply is poured back into the stock bottle. A few drops of water are now added to the vessel being cleaned. The resulting heat of dilution, concentrated in a small volume of residual cleaning solution, aids in a thorough cleansing of the glass surface.

Warning. All possible organic matter should be removed from a vessel by simple rinsing before an attempt to use chromic acid

cleaning solution. Should an appreciable amount of a reducing substance be present, as in a flask wet with alcohol, the entire quantity of the oxidizing component of the reagent will be destroyed in the single operation. Such misfortune is easily recognized the next day, when the cleaning solution is seen to be green instead of reddish brown.

9. Other Acid Mixtures. Occasionally mixtures of sulfuric and nitric acid have been used, and these may be of service to experts. Students are warned that concentrated nitric acid is a treacherous reagent when mixed with organic matter of questionable composition and may cause serious injury. Even the time-honored "aqua regia," standby for difficult tasks in inorganic qualitative analysis, is not recommended here and in any event is not only ineffective but decidedly offensive in the laboratory.

Incidentally, there is no substitute for intelligence in the application of any vigorous cleaning reagent to a given case. Witness the stock example of foolishness when one tries to remove the slaked lime from his absolute-alcohol apparatus with chromic-sulfuric acid. The chromic acid is useless, there being nothing to oxidize, while the sulfuric acid converts the lime into almost insoluble calcium sulfate.

10. Troublesome Cleansing Problems. Frequently organic matter in glass apparatus becomes scorched, perhaps so seriously that it is largely carbon, insoluble in all solvents. If the vessel is a Pyrex flask it may safely be cleaned by the following more drastic method:

Place about 1 g. of sodium or potassium dichromate and about 5 cc. of conc. sulfuric acid (or chromic cleaning solution) in the flask. Heat over a bare flame, spreading both flame and reagent evenly, until the acid fumes strongly. Under such circumstances both chromic and sulfuric acids will oxidize even free elemental carbon.

11. The Drying of Glassware. The good workman, having washed his glassware just after using it instead of waiting until he needs it again next week, may profit by the simple and obvious method of spontaneous drying. If, however, immediate drying is essential, a hot-air blast is convenient. A current of air is passed through a small iron device heated with a Bunsen burner, as shown in the accompanying figure. The outflowing air, at 150° to 200° C.,

is highly effective in drying laboratory glassware. For this purpose a reasonably dry source of compressed air is requisite. Furthermore, it is important that there be no oil spray in the compressed-air line from the lubrication system of the pump.

Pyrex ware may be dried upon the hot-air drier without special precautions against breakage. Test tubes, condenser tubes, and adapters will survive even though made of soft glass. Bottles require more care; do not allow the outlet tube from the heater to approach closely to the surface of a bottle. Dropping funnels or other ware carrying stopcocks must never be heated on the hot air drier!

12. Use of Volatile Solvents. Drying of glassware is expedited by a preliminary rinsing of the vessel with al-alcohol or acetone. A bottle of "wash alcohol" or "wash acetone" is kept on hand, and the contents are poured into a laboratory vessel only after the latter has been thoroughly cleansed, rinsed with water, and drained as completely as possible. The solvent wash liquid is then drained back into the stock bottle carefully.
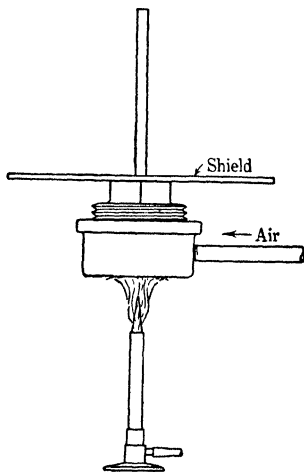
Fig. 1.   Hot-Air Drier

Warning. A fire or explosion hazard is possible when a flask rinsed with a volatile, inflammable solvent is placed on the hot-air drier. As shown in the illustration, the heater is provided with a large transite or asbestos shield which prevents an explosive solvent-air mixture from reaching the flame under the heater.

13. Drying by Evacuation. If no air heater is available, the vessel may be dried by cautious heating over a flame, followed by withdrawal of the hot moist air from the vessel with the aid of an aspirator. If compressed-air service is at hand, the moisture may be blown out. Finally, if really dry glassware is required, the final air supply introduced into the vessel must be first passed through a drying agent such as calcium chloride. Such extreme precautions are usually required only in special cases.

CORK AND RUBBER STOPPERS

14. Cork Borers. A student expecting to continue the study of chemistry beyond the present course is strongly advised to obtain an individual set of cork borers, running from $\frac{3}{16}$ to $\frac{1}{2}$ inch inclusive. The simplest style, as shown in Fig. 2, with removable steel pin as
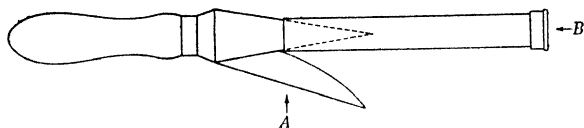
Fig. 2. Sharpening a Cork Borer

handle, is economical and permits sharpening more readily than the borer with permanent wing handle. Unless the laboratory is provided with special and frequent sharpening service, a cork borer for public use will not remain for long in fit condition to suit a good laboratory workman.

In any case frequent sharpening of a cork borer is required. Following the operation suggested in Fig. 2, take care that there should not be too great a pressure applied at A, lest the cutting edge of the borer be nicked; nor at B, lest the cutting circle be burst.

15. Cork Boring. Select a cork of ample size, as suggested in Fig. 3a. Roll it in a cork press until it is decidedly softened, and thus so that it will fit deeply and securely as represented in Fig. 3b. Do not attempt to bore a hole until the rolling operation is finished.

The size of the circular cutting edge of the cork borer should approximate the outside diameter of the tube that is to be inserted. Wet both borer and cork; if water is objectionable for the case at hand, use alcohol or glycerol. With a continuous rotary motion, cut a hole beginning at the small end of the cork. Remember that the borer is a cutter, not a punch, and do not allow it to burst its way through. As the borer advances through the cork, examine the tool from various sides several times to see that it is cutting a straight hole without slant. If much resistance is encountered, remove the borer and lubricate again. After the tool has been driven about halfway through, there are at least three rather different methods of completing the task as favored by different experienced workers.

(*a*) Holding the cork in the open between the thumb and two fingers, pass the cutter with gentle pressure and much rotation clear through the cork. This method is recommended only to the careful manipulator using a cork of high commercial grade and a well-sharpened borer.

(*b*) Remove the borer from the half-completed hole, and bore from the other end of the cork. If the two holes are carefully aligned, a neat aperture is assured with no torn or burst sections.

(*c*) Drawing an analogy from practice of the cabinetmaker: Stand the half-bored cork upon an old cork, and continue the boring operation until the opening is clear.

Do not press the borer into the desk or other hard object. Should the cutting edge of a brass tool be driven even once firmly against hardwood, it will require a special sharpening of the device on a lathe to restore its normal efficiency.

a   *b*
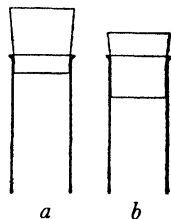
Fig. 3. Fitting
of Corks

16. Boring Rubber Stoppers. Frankly, it is much easier to bore a hole through a rubber stopper of cheap quality, or an old somewhat hardened specimen, than through a new, choice "pure-gum" stopper.

In any case, a somewhat larger borer is selected, in contrast with cork, and the tool is given the keenest edge possible. Glycerol is used as lubricant. The technique of rotary cutting instead of pushing is of more importance than ever because of the high elasticity of rubber.

Rubber is a hydrocarbon, and thus somewhat soluble in non-oxidized solvents such as benzene, alkyl chlorides, bromides, iodides, etc. Use of commercial rubber stoppers in experiments with these compounds is likely to give ill-smelling preparations.
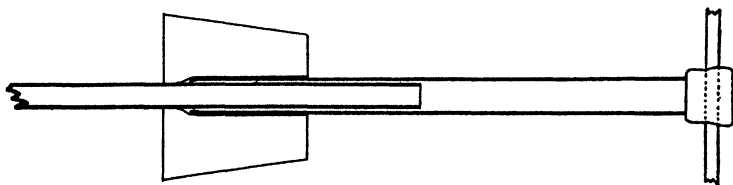
Fig. 4.   Removal of Tube from Rubber Stopper

17. Removal of Tubes and Thermometers. Many painful accidents have come from struggles to remove glass tubes from rubber stoppers. Figure 4 shows a convenient and safe method of removing such a tube by slipping the smallest possible cork borer over the tube. The borer should not be any sharper than necessary, and should be lubricated with soap solution or glycerol so that it will work its way into the passage without starting a new cut.

CHAPTER 3

Temperature Control

MEASUREMENT OF TEMPERATURE

18. Thermometers. The standard chemical thermometer with graduations etched in the stem is not a particularly rugged instrument. When the device is to be inserted in a stopper, care must be taken to grasp the stem close to the stopper, avoiding any prying leverage applied from a distance. Remember also that ordinary thermometers are not made of Pyrex glass and that they will not stand a plunge into cold water immediately after removal from a region of high temperature!

Ordinary chemical thermometers may be in error by a degree or more, owing to inaccuracy in graduation, irregularities in bore of tubing, or changes in the glass subsequent to manufacture. Corrections may be made with sufficient accuracy for use in the elementary organic laboratory with the aid of water and naphthalene, two substances readily obtainable in a high degree of purity. Melting and boiling points are tested; see §§ 183–187.

Calibration by Transition Temperature. Anhydrous sodium sulfate (Na_2SO_4), Glauber's salt ($Na_2SO_4 .10H_2O$), and water cannot exist in one mixture under ordinary laboratory conditions except at the temperature of 32.4° C. Should heat be added to this system, the following reaction proceeds to the right.

$$Na_2SO_4 . 10H_2O + \text{heat} = Na_2SO_4 + 10H_2O$$
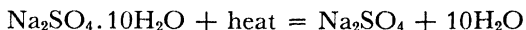
Should heat be withdrawn, the reverse reaction occurs. The temperature cannot rise or fall as long as all three components are present. If a thermometer be inserted in the mixture, it will soon register the constant temperature. Thus any possible error at the 32.4° mark is revealed. For this purpose 25 to 50 g. of the slightly moistened decahydrate, gently heated until partially dehydrated,

provides the equilibrium mixture cited in the equation above. The mixture, in the form of a thick slush, is well stirred with the thermometer under investigation.

19. Stem Correction. Unless a thermometer has been graduated in a special manner, as certified by appropriate markings, it is assumed that the manufacturer has followed the plan of "total immersion." That is, the entire thermometer is supposed to have been brought to the given temperature as that temperature was marked on the stem.

Assuming for simplicity a perfect graduation under total immersion, a reading will fall below the true value if a portion of the mercury column is outside the heated zone. It becomes necessary to add a correction value to show how much the protruding mercury column would rise if it were actually heated to the temperature of the medium under investigation.

The following formula yields the desired correction:

$$N(T - t)0.000154$$

in which N is the length of that part of the column which actually protrudes from the region of heating; T is the temperature of the thermometer bulb; t is the average temperature of the protruding column; and 0.000154 is a constant, which is the linear coefficient of expansion of mercury in glass.

In terms of actual laboratory practice, N is directly measured in degrees—that is, degree intervals indicating length. T is approximately, though obviously not precisely, the direct reading of the thermometer; while t may be found by placing a second thermometer with its bulb along side of the protruding stem of the main thermometer. The following example is illustrative.

A certain preparation of aniline boils at 182° (uncorr.). The temperature of the air is 30°, shown by a second thermometer hanging above. The bottom of the cork stands at the 90° mark.

$$N = 182 - 90 = 92 \quad \text{or approximately } 90°$$
$$T - t = 182 - 30 = 152 \quad \text{or approximately } 150°$$
$$90 \times 150 \times 0.000154 = 2.08 \quad \text{or approximately } 2° \text{ correction}$$

The boiling point of this aniline preparation is thus estimated, with accuracy sufficient for ordinary laboratory work, as $182 + 2$ or 184°.

20. Calibration for Partial Immersion. Certain thermometers are graduated for correct reading when they are immersed in a heated zone—such as a liquid bath—for a short and convenient distance only. A special mark is etched on the lower part of the stem, with the assumption that the user will immerse the instrument just to that mark and that the protruding stem will be at room temperature. While convenient, such thermometers are not ideal in theory, considering the great variation in temperature that is likely to occur in the space over the immersion boundary.

HEATING BATHS

21. Water or Steam Baths. It is frequently desirable to heat a laboratory vessel to temperatures up to 100° C., without risk of running to higher temperatures. If steam-cones, copper water baths, or like special devices are not at hand, ordinary sauce pans or open kettles will serve. Where no fire hazard is involved, a pan may be heated over the gas flame. If inflammable liquids are to be heated in a vessel placed in the water bath, the introduction of steam from piped laboratory service is to be recom-

Steam-Heated Water Bath

mended. The steam is led through a piece of commercial 5/16-inch copper tubing about 20 inches, or 50 cm., long. The tube is bent into the form of a loop as shown in the accompanying illustration. The entering steam, encountering the cold copper tube, condenses quietly without the disturbing noise produced when the steam enters through a tube of poorly conducting material such as glass or rubber.
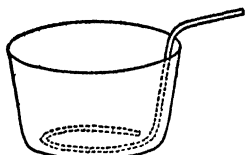
BATHS FOR HIGHER TEMPERATURES

22. Sand Bath. For controlled temperatures above 100° material less volatile than water must be chosen. In many laboratory directions written in Great Britain and on the Continent, the sand bath is often prescribed. Such a bath serves well as a support for the relatively fragile European flasks which were formerly the best available. Students using the more substantial borosilicate or Pyrex ware

should always consider the substitution of more convenient methods.

The principal shortcoming of the sand bath is seen in its lack of flexibility of control. When the sand bath becomes too hot, it may of course be removed; but it is not easily restored to position when needed again. Furthermore, the heat conductivity of sand is relatively poor.

23. Oil Bath. The use of a liquid instead of sand is much more convenient. Fusible-metal alloys, occasionally used, are generally too expensive and too heavy for the purpose, and oils serve to better advantage. Solid, "hard-hydrogenated" cottonseed oil (m.pt. about 60°) is perhaps the best available material, with technical stearic acid a close second. Common liquid vegetable oils, such as corn, cotton, rapeseed, and olive, have been used to some extent but have the disadvantage of high unsaturation of molecules and greater tendency to decompose; furthermore, being liquid at room temperature they are more troublesome to preserve and keep clean in the laboratory when not in use.

Petroleum products such as paraffin wax or lubricating oil are undesirable or even dangerous. Either they have high vapor pressures, as with paraffin or, if not so volatile, they are tarry and messy. The vegetable oils will not take fire under 300° C., whereas paraffin will flash and give a dangerous conflagration far below that temperature.

Hard cottonseed oil, heated to high temperatures, soon turns to a chocolate color and becomes opaque. Such discoloration does not ruin the material. Students are cautioned not to throw away any oil-bath contents without consulting the storekeeper. Care should also be taken to keep water out of the oil to avoid disconcerting or even dangerous crackling and splashing of the hot liquid. Should water get into the oil, the remedy is simple if the oil is of the "hard" variety; simply allow to cool and solidify. Finally crush the brittle solid and expose to dry air.

Where still higher temperatures are desired (250° to 500°) a mixture of equal weights of solid sodium and potassium nitrates may be used, but with care not to allow any combustible matter to get into the molten salt mixture.

For baths used in melting-point apparatus see § 147.

24. Reflux Condenser. The simplest method of maintaining a fixed temperature in a liquid reaction mixture is to boil the material. As fast as the solvent boils away, the vapor is recondensed in a reflux condenser. As the name suggests, the condensate runs back into the boiler.

The process of "refluxing" may at least theoretically continue in-
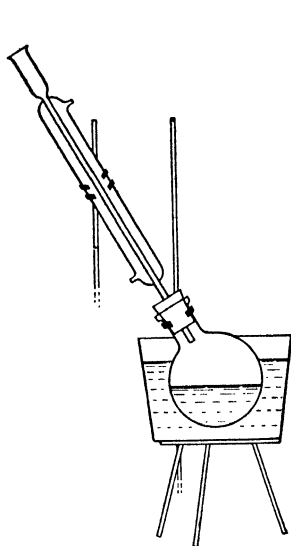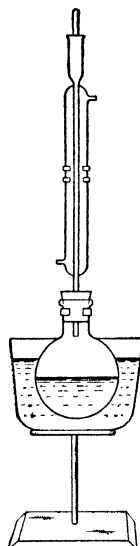
Fig. 1   *Fig. 2*

Arrangements of Reflux Condenser

definitely, provided the cooling stream through the condenser is adequate and special care is taken to prepare a vapor-tight union in the rolling and boring of the cork holding condenser to flask. The lower end of the condenser should project 2 cm. or more below the stopper, but not down into the body of the flask.

The oblique mounting of the condenser shown in Fig. 1 is safer than the vertical arrangement of Fig. 2 when an inflammable liquid is being refluxed since the flow of condensate passes more rapidly and certainly into the boiling flask. In the outfit of Fig. 2, with active boiling of the liquid, it is possible for a column of liquid to accumulate in the condenser. A sudden spurt of vapor may blow this

liquid entirely out of the apparatus.   The expelled liquid falls directly upon the flame, and a fire is almost certain.

Some condensers are manufactured with a constriction at the delivery tip.   This design is to be condemned, since it helps to cause accidental fires like that described above.   If the condenser tip is provided with a beveled end, is unconstricted, and the rate of boiling is moderate, the vertical arrangement of Fig. 2 is recommended. The vertical mounting is more compact, uses but one ringstand, and permits easy attachment of a ring instead of the less desirable, disconnected tripod.   Organic chemists have sharp differences of opinion, however, on the question of angle of mounting.   When the refluxed liquid boils above 150° an air-cooled condenser may be used. A Liebig condenser not served by a stream of water is not a substitute for the simple air-cooled device.   Its empty outer jacket would serve as a heat insulator rather than as means for cooling.

The service of the refluxing operation as a simple means of stirring a reaction mixture may not be satisfactory in a two-liquid-phase system.   If the denser of the two liquids, lying on the bottom, happens to be a high-boiling liquid, only the top layer will be stirred by bubbles.   One then may resort to a motor-driven stirrer.

25. Baths for Low Temperature.   Finely crushed ice in water is convenient for maintenance of temperatures in the vicinity of 0° to 5° C.   A substantial addition of dairy salt to the crushed ice will give, in practice, temperatures from $-15°$ to $-5°$, theoretically as low as $-21°$ C.   Although still lower temperatures may be attained by the use of calcium chloride or other inorganic compounds in place of the salt, modern workers prefer suspensions of solid carbon dioxide (dry ice) in alcohol or like solvent.   Such mixtures easily reach $-50°$ C.   They are of particular value in trapping out harmful vapors which should be excluded from a vacuum pump in reduced-pressure distillation.   (See § 35.)

Questions

1. State two reasons why stem correction is more important in the distillation of high-boiling than of low-boiling liquids.

2. Calculate the thermometric stem correction for a liquid being distilled under the following conditions: bottom of the cork at the $-20°$ mark; reading of the thermometer 85°; temperature of the air outside 30°.

3. Suppose that the outfit mentioned in question 2 were operated at reduced pressure, resulting in a thermometer reading of 10° instead of 85°. Calculate the stem correction.

4. A thermometer was correctly graduated for partial immersion, with the mark for immersion set at −10°. Suppose the instrument were completely immersed in pure liquid naphthalene, boiling at 760 mm. pressure. What would be the reading of the thermometer? (See § 446.)

5. In which case do you think the water-cooling operation in a condenser is more efficiently carried out, when the condenser is attached in the normal position for distillation as in Fig. 1, § 33, or in the reflux position? Why?

6. Sketch an outfit which might be used to keep a reaction mixture constantly at 118°, given a small supply of n-butyl alcohol (b.pt. 118°).

7. Why is it safer to heat a nonvolatile organic reaction mixture in an oil bath rather than over ordinary wire gauze?

CHAPTER 4

Calculation of Quantities of Materials

26. In preparing exact directions for synthesis of an organic compound, one should first write a complete balanced equation showing the transformation of the starting materials into the product. For example, when phthalic anhydride is heated with resorcinol (see § 380), fluorescein is produced.

Phthalic anhydride   resorcinol   fluorescein

$$C_6H_4(CO)_2O + 2C_6H_4(OH)_2 \rightarrow C_{20}H_{12}O_5 + 2H_2O$$
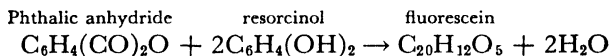
With careful technique this reaction proceeds practically to completion, without concern over by-products. Quantities in agreement with the equation are therefore chosen: 7.5 g. of the anhydride (0.05 mole) and 11 g. of resorcinol (0.1 mole).

27. Altering of Proportions. Frequently a reaction does not proceed in as simple a manner as indicated above. Reasons arise for choosing other than the theoretical proportions of raw materials. For example:

(*a*) One of the reagents may be of such character that it is likely to be partially wasted during the process, in spite of careful manipulation. Perhaps the reagent is slowly oxidized in an undesired side reaction. In other cases the reagent may be a volatile liquid, like methyl alcohol (b.pt. 65°) which is inexpensive as well as prone to escape by evaporation. An excess of such a reagent is then prescribed.

(*b*) The reaction employed in the synthesis may be one which runs to equilibrium. It is desirable to drive it more nearly to completion than normal conditions permit; wherefore an excess of one reagent is used. The substance used in excess is usually one which is inexpensive, or one of which the superfluous residue is easily removed, and perhaps reclaimed, at the end of the reaction period. Usually the excess reagent is eliminated by distillation or washing.

(*c*) Occasionally one of the reagents is of a type difficult to remove from a reaction mixture in which some of it might survive as a residue. It is thus desirable to use an excess of the second reagent to make certain that the consumption of the first will be complete.

Sometimes the purity of a reagent is uncertain. Such diverse materials as isopropyl alcohol, sodium dichromate, hydrochloric acid, glycerol, etc., have varying amounts of water in their common commercial forms. An excess may thus be desirable.

28. Calculation of Yield. The theoretical yield in an organic synthesis is that quantity of product called for by ordinary chemical arithmetic under the particular directions employed. In the simple case of fluorescein the equation shows directly that one mole of fluorescein is produced from one mole of phthalic anhydride and two moles of resorcinol. Hence 0.05 mole, or 16.6 g., of fluorescein is the largest amount which could possibly come from the quantities of reagents actually used in the experiment. The theoretical yield is thus 16.6 g.

Usually, however, deviations from theoretical proportions make it necessary to decide which reagent is to serve as the basis of calculation.

Example. Sixty grams of *n*-butyl bromide was heated with 15 g. of metallic sodium (Wurtz reaction), and 20 g. of *n*-octane was obtained as a product.

$2C_4H_9Br$	$+ 2Na$	$\rightarrow$	C_8H_{18}	$(+ 2NaBr)$
2 moles	$+$ 2 gram-atoms	$\rightarrow$	1 mole	——
274 g.	$+$ 46 g.	yields	114 g.	(Theory)
60 g.	$+$ 15 g.	yielded	20 g.	(Practice)
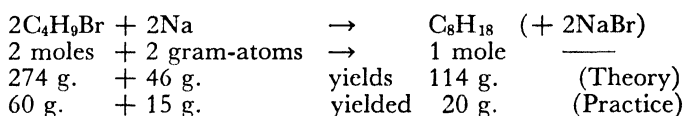
One may now arbitrarily select either experimental quantity of starting material (60 or 15) for numerical test of the specifications. For example, the 60-g. value is selected. If 274 g. of *n*-butyl bromide requires 46 g. of sodium, solution of a simple algebraic proportion will determine the maximum quantity which could react with 60 g. of the bromide:

$$\frac{274}{46} = \frac{60}{x}$$

$$x = 10.1 \text{ g. of sodium required by theory.}$$

Obviously the 15 g. of sodium actually prescribed in the experiment was an excessive quantity. Part of the reagent must have been

left over, and thus the full original weight has no place in the calculation. A homely analogy is seen in the calculation made by a manufacturer who has just received a rush order for the maximum possible output of bicycles from his assembly plant. Inventory shows 218 wheels and 152 frames in stock. A simple common-sense calculation leads to prompt rejection of the figure 152 as a numerical basis for immediate sales. Similarly, the experienced chemist usually decides such cases in the chemical field with a rough, common-sense computation.

Butyl bromide is the limiting factor in the example—the substance of which the supply is short. The problem is thus simplified—How much octane can be made from 60 g. of butyl bromide?

Sixty grams of butyl bromide is $60/137$ mole. Since two moles of the bromide yield, by theory, one mole of octane, $60/137$ mole of bromide will yield $1/2 \times 60/137$ mole, or $30/137$ mole (25 g.) of n-octane. Only 20 g. of octane, however, was actually obtained. The "percentage yield" is therefore $20/25$ or 80%.

29. Three Starting Materials. If a synthetic process calls for three different reagents, any two are first taken at random for consideration. As described in the octane example just given, one of these is rejected as present in excess. The other is compared with the third reagent, and a decision made as to which of these is present in scant supply, and thus is to be the basis for calculation. The illustration outlined as a sample card report in § 2 is an example.

C_3H_7OH + KBr + H_2SO_4 → C_3H_7Br + $K^+HSO_4^-$ + H_2O
60 g.   119 g.   98 g. → 123 g.   ——   (Theory)
40 g.   60 g.   100 g. → 48.5 g.   ——   (Practice)
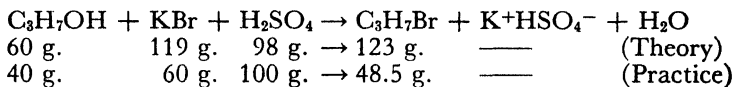
With propyl alcohol and potassium bromide first chosen for comparison, the following is solved.

$$\frac{60}{119} = \frac{40}{x}$$

$x = 79.3$ g. of KBr theoretically required for 40 g. of the alcohol.

But no such quantity as 79.3 g. is available. Only 60 g. was provided. Therefore the 40 g. of propyl alcohol cannot be used up, and so propyl alcohol is stricken out of the calculation.

Potassium bromide and sulfuric acid are left for consideration. Again a proportion may be set up, this time with the terms 119, 98,

60, and *x*. By this time, however, the reader should be able to decide on rapid inspection that the sulfuric acid has been prescribed in theoretical excess, and thus that it should be stricken out of calculation. Potassium bromide remains as the limiting factor, the substance present in relatively scant quantity. The final calculation is seen in § 2.

BALANCING OXIDATION-REDUCTION EQUATIONS

30. Method of Positive and Negative Valences. In view of the numerical complications in many equations involving oxidation, a systematic plan of balancing an equation is desirable. The valence method, familiar to many students in inorganic chemistry, has special value here because it aids in a better understanding of the important concept of the oxidation states of carbon compounds.

In this plan the graphic formula is first examined for the purpose of determining the valence state of the carbon atom or atoms which take part in an oxidation reaction. If one of the carbon bonds holds hydrogen, such is counted as a negative valence, and this incidentally means a reduced state and fuel value. If the bond holds oxygen, it is counted as positive, meaning an oxidized state and absence of fuel value. For example, the valence of carbon in methane, CH_4, is -4; in CO_2, the opposite extreme, $+4$; in acetic acid, CH_3COOH, the total valence of carbon is 0, which here is derived by algebraic addition of -3 and $+3$. In ethyl alcohol, C_2H_6O, the relatively high negative valence total of -4 is observed, meaning that this compound is a good fuel, though not equal (per gram) to methane; while oxalic acid, $C_2H_2O_4$, yields a valence total of $+6$, indicating poor fuel value, but not quite as low as CO_2.

The explanation is often given that the compounds rated above in the negative-valence class have more available electrons, while those with positive carbon atoms have lost electrons. While this is true in a physical sense, the electron count is at times confusing and offers no convenience in the immediate task at hand, namely, the actual calculation of quantities needed. A valence count is simpler.

Example. What quantity of potassium permanganate is theoretically required, in the presence of sulfuric acid, to convert 58 g. of ethyl butyl carbinol into propionic and butyric acids?

First represent graphically the exact changes which take place, preserving similar positions (on paper) for all carbon atoms before and after reaction. It is now convenient, especially with large molecules reacting at only one restricted location, to draw enclosing lines about all carbon atoms in the molecule of the starting material which are said to be undergoing oxidation, or change in valence. Similarly enclose the same carbon atoms in the product or products.

$$
\begin{array}{ccccccc}
H & H & H & \boxed{\begin{array}{cc} H & H \\ C-C \\ H & O \\ & H \end{array}} & H & H & \\
HC-C-C- & & & & -C-CH + KMnO_4 + H_2SO_4 \rightarrow \\
H & H & H & & H & H &
\end{array}
$$

$$
\begin{array}{cccc}
H & H & H & \\
HC-C-C- & \boxed{\begin{array}{c} O \qquad O \\ /\!/ \qquad \diagdown \\ C \qquad\qquad C \\ \diagdown \qquad / \\ OH\ HO \end{array}} & \begin{array}{c} H \quad H \\ -C-CH \\ H \quad H \end{array} + K^+ + Mn^{++} + SO_4^= \\
H & H & H &
\end{array}
$$
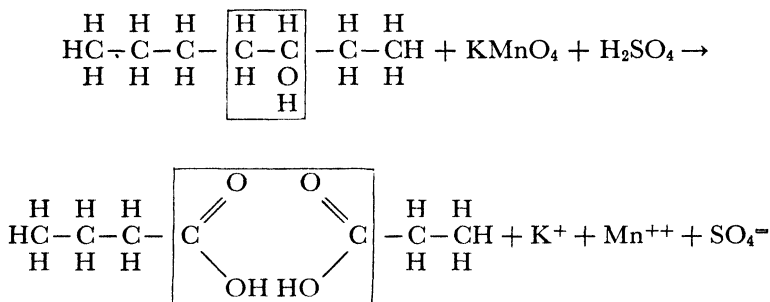
Since there is no concern at the moment about any parts of the molecules outside of the two enclosures, no valence count of such external atoms is necessary. A simple count inside shows the change in valence from start to finish. Only this change is important.

The total valence of the carbon atoms in the upper enclosure reaches the algebraic sum of -2, meaning that these carbon atoms have three negative valences (holding hydrogen) and one positive (holding hydroxyl). (Valences between carbon atoms have no significance in this sense, positive or negative, and may be overlooked as of zero value.) In the product, however, the algebraic sum of valences for those same carbon atoms is $+6$, all holding oxygen.

Since the reacting carbon atoms change in valence from -2 to $+6$, eight electrons must have been given up, and thus eight equivalents of oxidizing agent are required per mole of alcohol. Permanganate ion, on the other hand, in changing to manganous ion, has an oxidizing equivalent of five, the manganese gaining five electrons and changing from a valence of $+7$ to $+2$. It is thus necessary to use eight moles of permanganate to oxidize just five moles of the alcohol. This leads to the following incomplete expression, which merely shows the bare essentials of oxidation.

$$5C_7H_{15}OH + 8KMnO_4 \rightarrow$$
$$5C_3H_7COOH + 5C_2H_5COOH + 8K^+ + 8Mn^{++}$$
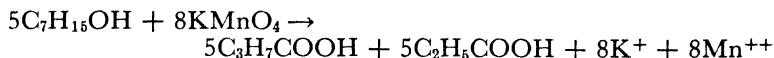
The last two terms indicate the necessity of procuring negative ions from some source, to the total electrical equivalent of $8 + 16$, or 24 minus charges. Sulfate ion is the only available material for the purpose, and thus 12 molecules of H_2SO_4 are needed.

$$5C_7H_{15}OH + 8KMnO_4 + 12H_2SO_4 \rightarrow$$
$$5C_3H_7COOH + 5C_2H_5COOH + 8K^+ + 8Mn^{++} + 12SO_4^=$$

When the oxidation has been correctly balanced and the necessary ionic material furnished, nothing remains but the addition of water and the assemblage of inorganic ionic components into complete molecular form if such is desired. A mere inventory of atoms shows the necessity here of 17 molecules of water as a product, leading to the final equation,

$$5C_7H_{15}OH + 8KMnO_4 + 12H_2SO_4 \rightarrow$$
$$5C_3H_7COOH + 5C_2H_5COOH + 4K_2SO_4 + 8MnSO_4 + 17H_2O$$
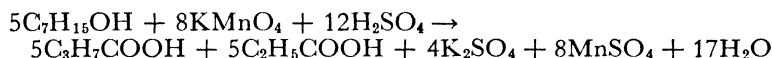
Only 58 g., or 0.5 mole, of the carbinol was given in the original example, however. Eight-tenths mole of permanganate and 1.2 mole of sulfuric acid are thus required.

31. Short-Cut Method. The valence change in the organic reagent may be determined by the simple arithmetical trick of adding (algebraically) the valences of all the hydrogen and oxygen atoms in starting material and product respectively. Only simple condensed or molecular formulas are needed:

$$C_7H_{15}OH \rightarrow C_3H_7COOH + C_2H_5COOH$$
$$(15 - 2 + 1) \rightarrow (7 - \underbrace{4 + 1) + (5 - 4}_{} + 1)$$
$$14 \quad \rightarrow \quad \underbrace{\qquad 6 \qquad}$$
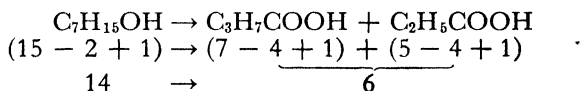
The change of 14 to 6 indicates a loss of eight electrons, requiring eight equivalents of oxidizing agent. The rest of the calculation proceeds as already outlined in § 30. This short-cut is trustworthy only when no other element than hydrogen or oxygen leaves the organic compound during the oxidation.

32. Method of Separate Equations. Many organic chemists prefer to separate the oxidation and reduction reactions, using hypo-

thetical free atoms of oxygen as an arithmetical device to aid in ultimate combination of the two parts. First an oxidizing agent yields (hypothetically) oxygen atoms; then the reducing agent takes the appropriate number of these. For convenience in comparison, the oxidation of ethyl butyl carbinol is again chosen, as cited in § 30.

(*a*) Oxidizing Agent:

$$2KMnO_4 + 3H_2SO_4 \rightarrow K_2SO_4 + 2MnSO_4 + 3H_2O + 5(O)$$

(*b*) Reducing Agent:

$$C_7H_{15}OH + 4(O) \rightarrow C_3H_7COOH + C_2H_5COOH + H_2O$$
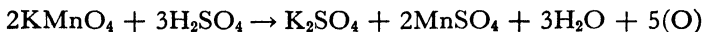
It is now the aim to add these two equations in such a manner that the terms (O) shall disappear. This is easily prearranged by multiplying the terms of (*a*) by the factor 4, and those of (*b*) by 5.

$$8KMnO_4 + 12H_2SO_4 \rightarrow 4K_2SO_4 + 8MnSO_4 + 12H_2O + 20(O)$$
$$5C_7H_{15}OH + 20(O) \rightarrow 5C_3H_7COOH + 5C_2H_5COOH + 5H_2O$$
$$\overline{8KMnO_4 + 12H_2SO_4 + 5C_7H_{15}OH \rightarrow}$$
$$4K_2SO_4 + 8MnSO_4 + 5C_3H_7COOH + 5C_2H_5COOH + 17H_2O$$
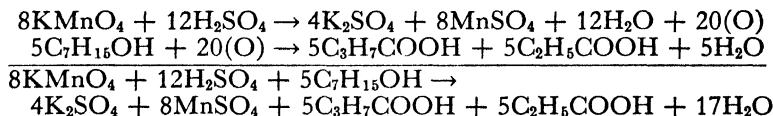
Similar methods of calculation may be carried out for reductions of organic compounds; for example, in the conversion of nitrobenzene to aniline, where nitrogen is involved instead of carbon.

Questions

1. If four reagents were required in a mixture used for organic synthesis, how would you decide which of the four should serve as a basis for calculation of theoretical yield?

2. Benzene (780 g.) was chlorinated, yielding chlorobenzene (562 g.) and *p*-dichlorobenzene (294 g.). Calculate the percentage yield.

3. Suppose ethylene is converted (*a*) into ether, (*b*) into acetaldehyde. In terms of the valence state of carbon atoms, is the reagent oxidized in either case? Prove your answer numerically.

4. What quantity of potassium permanganate is required, in the absence of sulfuric acid, to convert 15 g. of *n*-propyl alcohol into potassium propionate? What happens to the manganese in this reaction?

5. What quantity of potassium dichromate is required in the presence of sulfuric acid to convert 37 g. of sec.-butyl alcohol

(*a*) into the ketone?   (*b*) into acetic acid?

6. In the presence of acid, how many gram-atoms of zinc are required by theory to convert one mole of nitrobenzene into aniline?

7. If the reduction of nitrobenzene by zinc is conducted in alkaline solution, zincate ion (ZnO_2^-) and hydrazobenzene, $C_6H_5 . NH . NH . C_6H_5$ are produced. What quantity of zinc would be required in this case to reduce one mole of nitrobenzene?

CHAPTER 5

Technique of Distillation of Liquids

33. Distillation at Atmospheric Pressure. Figures 1 to 5 illustrate common arrangements of standard apparatus for distillation. Other combinations of flask, condenser etc., are possible.

The ringstand rods supporting this glassware should stand directly back of the respective pieces. This enables clamps to point directly outward and lie perpendicular to the condenser tubes, side stems, and general line of the apparatus. After such careful right-angle layout one may readily tilt condenser and flask upward or downward so that the delivery end reaches a position at convenient distance from the desk. Although the distilling flask is best fixed in a vertical position, a slight tip to the left or right does no essential harm.

Flask, condenser, and receiver should be independently placed, with such clamps as are necessary, in as nearly the correct position as possible—then slipped together to proper fit. The common practice by the novice of clamping a distilling flask tightly and then trying to fit its side stem to an unsupported condenser frequently ends in grief. The side stem snaps off.

Pieces of rubber tubing should be fitted upon the jaws of clamps that are to hold glassware. Inasmuch as rubber is easily damaged by heat, such glassware, particularly the boiling flask, should be clamped at the coolest place that is practicable. Normally this means above the side stem, despite the fact that the clamp is distant from the center of gravity of the system. With air-cooled condensers (Fig. 2) asbestos paper may well be substituted for the rubber on clamp jaws.

FIRE HAZARDS IN DISTILLATION

34. Inflammable Solvents. Liquids which introduce fire hazards during distillation may be divided roughly into three classes.

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 5

31
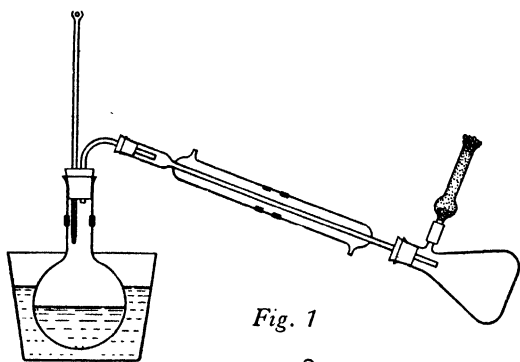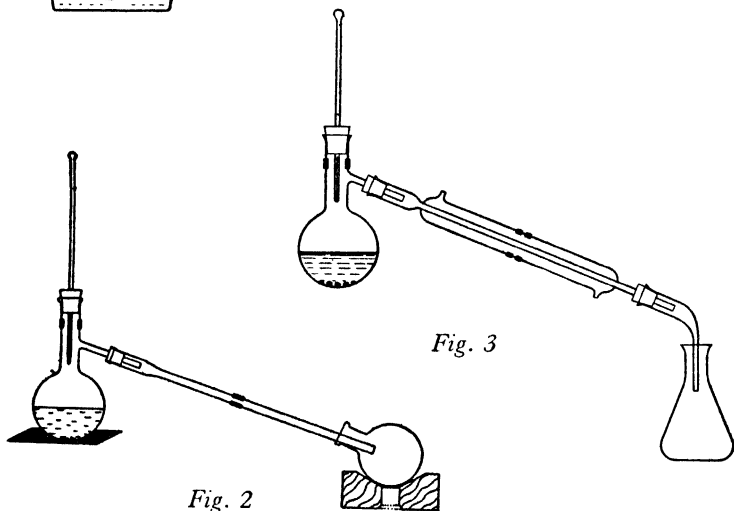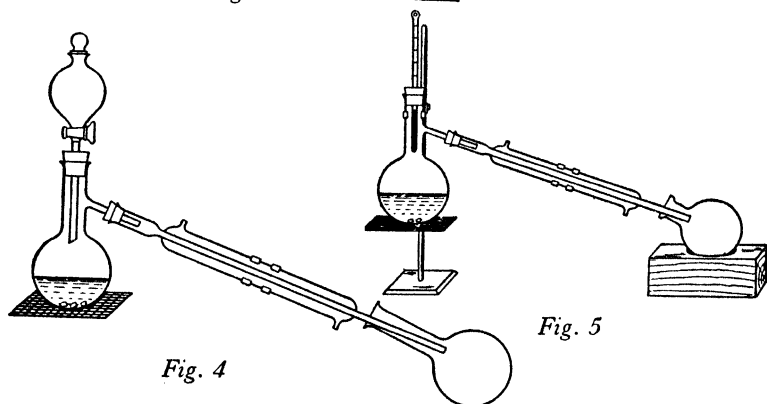
(a) *Diethyl Ether, Petroleum Ether.* These solvents, with boiling points below 50°, are dangerously inflammable. No flame whatsoever is permissible under or near the distilling apparatus. Even a flame as much as 10 feet distant may ignite ether if a continuous tabletop lies between the flame and the exposed ether and a gentle draft is blowing in the appropriate direction.

Either use piped steam service or bring a supply of boiling water from a distance. In research operations, or wherever the expense is warranted, special electric hot plates, in which the heating elements are thoroughly covered, may be used to distil ether.

Special Warning. Carbon disulfide (b.pt. 48°) might be placed in class (a), but actually is more dangerous. This treacherous solvent may ignite from the surface of a hot plate or even from a steam radiator. If it is necessary to distil carbon disulfide in the laboratory, use a water bath and bring warm water (60° to 80°) from a distance.

Ether that has stood for some time may contain an explosive impurity; see § 89.

(b) *Benzene, Ethyl and Methyl Alcohols, Di-isopropyl Ether.* These solvents, intermediate in volatility between ordinary ether and water, may of course be distilled most safely by the method described in (a) above. The piped steam service, however, may be replaced by a gas-heated water bath. An outfit similar to that shown in Fig. 1, § 33, is used, but the calcium chloride tube is replaced by a length of gas hose. The open outer end of this hose is allowed to hang over the edge of the desk. If through oversight, or failure of condenser water service, the inflammable vapors are not properly condensed before entering the receiver, they escape from the hose at a point where ignition is unlikely. Methyl alcohol (b.pt. 65°) and di-isopropyl ether (68°) deserve special care of this kind.

Unfortunately the steam bath, while satisfactory for distillation of the above solvents when they are in a comparatively pure state, is often not adequate for complete expulsion of these liquids from their mixtures with less volatile liquids. For example, in later situations the need will arise for elimination of di-isopropyl ether from extracts. For example, see phenol, § 309. The boiling point of an ethereal extract of such a liquid will gradually rise from its initial value near 68°. Before the ether has all passed over, however, the temperature approaches 100° so closely that distillation practically ceases. It is now necessary to change from steam heat to the gas

flame. Before this change is made, however, the main yield of recovered ether, already in the receiver, is removed to a safe distance and placed in a stoppered bottle.

The steam bath is now replaced with wire gauze, and a gas flame is applied to the distilling flask. Any possible fire from this point on cannot be very serious, since the residual ether is of small volume.

(c) *Toluene* (*b. pt. 111°*). Inflammable solvents with boiling points above 100° of course cannot be distilled from the steam bath. In a case like that of toluene, a Pyrex distilling flask, immersed in an approved oil bath, may be employed, preferably in fireproof quarters. The flask is connected to the water-cooled condenser, stoppered filter-bottle, and rubber tube hanging from the desk, as described in (b) above. The oil bath is of course gas-heated.

With such an outfit the danger of cracking and downfall of the distilling bulb and its inflammable contents is practically nil. Ordinarily an oil bath will not cause the "scorching" and adhesion of organic matter and consequent cracking of glass (see § 23). Admittedly there is still chance for a big fire in case of gross carelessness, but not such a personal hazard as would exist if flaming toluene fell upon the table and splashed. If he must distil quantities of such a solvent, the student is warned to make sure of the location of fire extinguishers before starting operations.

DISTILLATION UNDER REDUCED PRESSURE

35. Safety Precautions. In view of the hazard of collapse of an evacuated flask, with a pressure of nearly 15 pounds per square inch upon its entire surface, goggles or stout wide-rimmed spectacles are worn during reduced-pressure distillation. Particular care is also taken that there be not the slightest crack or other defect in the distilling flask. No flat-bottomed ware is admissible. Pyrex flasks are particularly desirable.

The assembly of flask, receiver, and funnel, as shown in Fig. 1, is connected either to the accessories shown in Figs. 2 and 3 or to those of Fig. 4, according to the type of pump used. If a filter pump is employed, the outfit of Fig. 2 or 3 is appropriate. In this arrangement a safety bottle is essential to protect the apparatus from back flow of water. If a mechanical pump is used, the safety bottle is of less consequence, but a new difficulty arises. Vapors from the

distilling flask may pass into the pump, condense, and cause not only undesirable dilution of the pump oil but corrosion of metal parts. To prevent such an occurrence, the vapors from the main section of the apparatus are caused to pass through a trap (Fig. 4) immersed in a suspension of dry ice in alcohol. Reduced-pressure distillations should never be conducted with an unprotected motor-driven pump!

36. Use of Capillary Tube. The two-necked Claisen flask permits the introduction of a capillary tube required to furnish a minute but steady supply of air to facilitate bubbling. The capillary tube is prepared from a piece of common glass tubing selected primarily because it fits the stopper well. This tube is heated strongly in a blast or efficient wing flame and drawn out until it is so fine that only a negligible volume of air can get through even at full pressure. It should be tested to prove that there really is a free passageway by dipping the tip in ether or acetone and attempting to blow bubbles through the liquid. When finally mounted, the tube should reach nearly to the bottom of the flask.
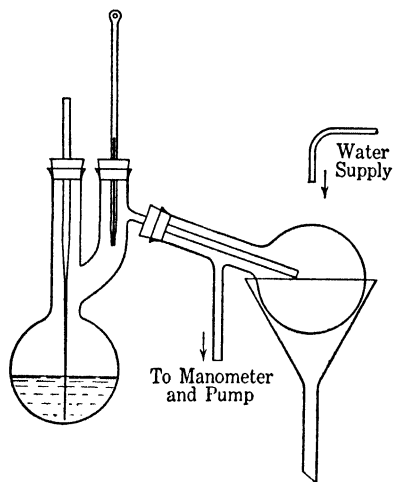
Fig. 1. Apparatus for Reduced-Pressure Distillation

The side stem of the flask should pass well into the bulb of the receiver to prevent diversion, or short circuit, of uncooled vapors over into the manometer and pump. The outside of the receiver should be gently scrubbed with household abrasive washing powder just before the distillation is started, so that the stream of cool water will cling to the glass and spread properly over its surface. Either a water bath or oil bath, according to temperature requirements, should be used, not wire gauze. Bumping is minimized by such procedure. When bumping is particularly troublesome, some operators place a loosely bunched mass of glass wool in the bulb of the Claisen flask.

It is usually easier to maintain good vacuum when rubber stoppers are used, but the disadvantage of ill-smelling sulfur derivatives from heated rubber applies here as in ordinary distillation. Careful workers, using well-rolled and well-bored corks, have no real trouble in reduced-pressure distillation. Some experimenters recommend a light, superficial charring of the corks before seating in the necks of flasks. Others use synthetic lacquer-like cements, or even glycerol or castor oil, on the surface of the cork before insertion.

37. Efficiency of Pumps. The common aspirator or filter pump, operated by domestic water service, is generally employed for evacuation of reduced-pressure apparatus if no very low pressures are required. In mild weather such a pump will permit distillation at a minimum of about 20 mm. Theoretically the aspirator reduces the pressure in the system to a value equal to the vapor pressure of the water passing through the device. For example, at 14° C. (57° F.) the vapor pressure of water is 12 mm. This leaves a margin of 8 mm. to allow for heat of the laboratory and leakage of air into the apparatus.

Fig. 2   Fig. 3

Manometers

In winter, with a water supply coming directly from under ice, a theoretical minimum of 4.57 mm. is obtainable; in practice about 8 mm. In summer it may be difficult to lower the pressure below 30 mm.

Mechanical pumps, oil-immersed, are used for lower pressures.
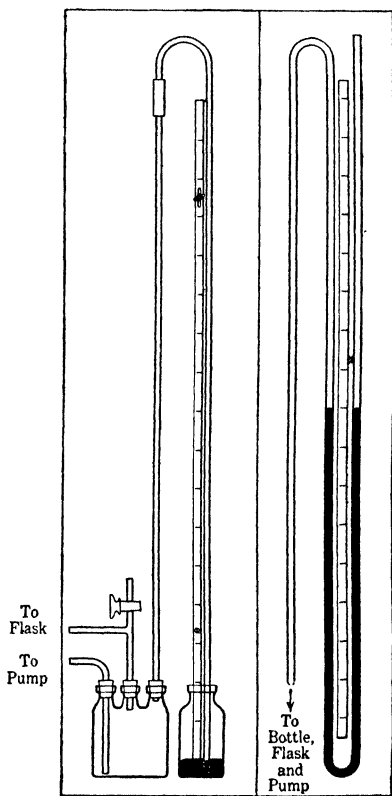
For common distillations it is not necessary to use the high-vacuum appliances popular in physics, which evacuate to 0.001 mm. Pumps handling large capacity at moderate pressures (0.1 mm. is ample) are more suitable.
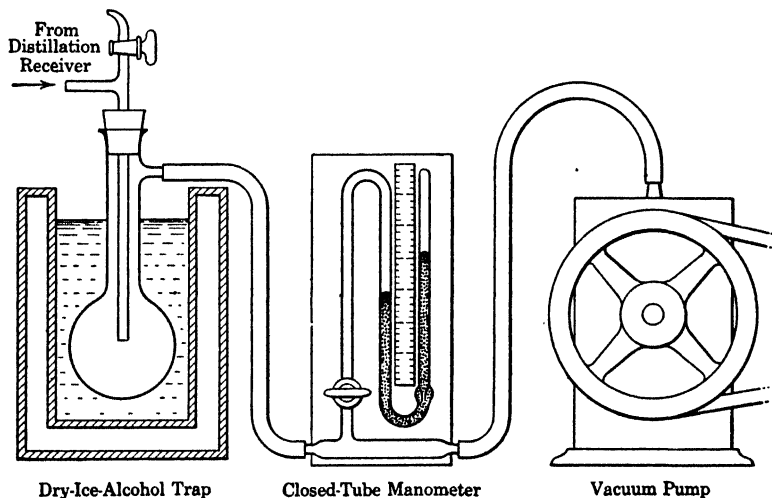
Fig. 4. Apparatus for Low Pressures

38. Manometers.   Among devices for measuring the pressure during a distillation, the two similar models illustrated in Figs. 2 and 3 are probably the best, certainly the most rugged, for beginners. In either case the vertical tubes must be slightly more than 760 mm. long, resulting in a total assembly of somewhat awkward size. A wall mounting is often desirable. The model shown in Fig. 3 is neater, but not so readily cleansed as that of Fig. 2.

Experienced workers, who are careful not to allow condensable vapors to reach a manometer, use more compact, closed-tube de-vices, as illustrated in Fig. 4. Such manometers have the advantage over the longer models in that the pressure of the system is read off directly by measurements of difference in level of the adjacent mercury columns. With the devices of Figs. 2 and 3, however, such difference in level must be compared with the barometer reading in the laboratory. On the other hand, if the slightest quantity of vapor reaches the closed space of the short manometer, all readings are

thrown into error. This handicap is not a feature of the tall models. The access of such vapor to the short manometer is minimized by the constricted ring-sealed insert shown in Fig. 4.

For discussion of the theory of reduced-pressure distillation, see § 52.

DISTILLATION WITH FRACTIONATING COLUMN

39. Ordinary Laboratory Columns. The simplest form of fractionating column consists of a vertical glass tube interposed between the mouth of a boiling flask and the entrance to a condenser. Only part of the vapor passing into this tube reaches the condenser and forms the distillate. The remainder returns to liquid form in the column, falls back into the boiler, and is called the condensate. As suggested in § 75, the column is not efficient unless it contains a succession of partial obstructions, circuitous passageways, or other devices to aid in separation of components in the liquid being distilled. A great deal of ingenuity has been expended in details of construc‧ tion.

The **Hempel column** is perhaps the simplest to prepare. The "packing," as it is sometimes called, consists of glass beads. These should not be ornamental beads with fine needle holes, but are best made by cutting short sections of glass tubing. Such ready-cut material is available commercially. The column should have indentations at the bottom to prevent beads from falling through.

The **Vigreux column** has the advantage of easy washing, no loose parts to fall out, and less holdup of liquid during fractionation. It is not as efficient as the Hempel, however, because there is less opportunity for liquid and vapor to be thoroughly intermixed.

40. Special Columns. In recent years an extensive new offering of highly efficient fractionating columns has been presented in the American market. These devices feature special forms of packing, and usually employ the modern standard-size all-glass ground joints, eliminating rubber and cork. In such columns the main vertical tube, or body of the column, is slender. In order to afford the stable thermal environment necessary for steady, efficient fractionation, the column proper is surrounded with heat-insulating material or with an outer tube used as a jacket. The space between the jacket and the central column may be evacuated or may be equipped

with an electrical resistance heater. The heater is particularly favored in conjunction with a variable-voltage transformer, which may be adjusted neatly to give the proper input of heat, and thus precisely the vapor output desired at the top of the column.

In certain columns used extensively in petroleum analysis, a single closely wound, tightly fitted wire spiral constitutes the sole packing. The tube is only 4 to 7 mm. inside diameter. The famous Podbielniak models illustrate such design. Aside from glass beads and wire spirals, such material as coarse carborundum crystals and glass helices have been found effective as packing. The helices, which consist of single turns broken from a fine cylindrical glass spiral, expose a maximum of liquid surface under operating conditions with a minimum of holdup in the column. Figure 6 shows a column employing glass helices.
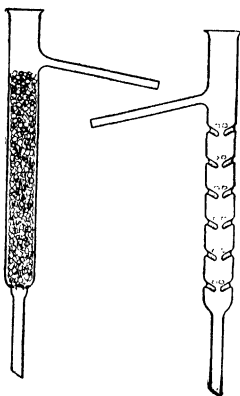
Fig. 5. Hempel and Vigreux Fractionating columns

41. Efficient Fractionation. When sharp separation of components is desired, the rate of accumulation of distillate must be slow; otherwise there would not be time for the desired exchange of components between vapor and liquid in the successive zones of the column (see § 75). It would then seem desirable to moderate the intensity of heating under the boiler so that only a small vapor output would finally make its escape through the top of the column. Such an adjustment is very unstable; the slightest drop in the heating stops the distillation. An increase in the heat is likely to cause excessive output and a breakdown of fractionation.

42. Total Reflux Method. One of the best methods of meeting the difficulty of irregular and unstable fractionation provides a small reflux condenser mounted on the top of the column, as shown in Fig. 6. The apparatus is operated so as to send a substantial and thus stable current of vapor from the top of the column. This large output is totally refluxed. A small part of the refluxing liquid, however, is allowed to pass into the receiver, the stopcock providing the necessary control of quantity. The balance runs back into the column. The reflux ratio, between flow back to the column and
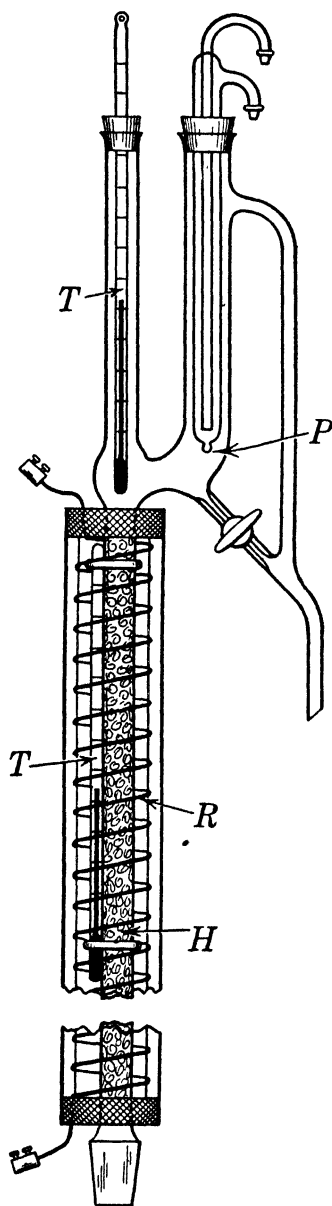
*Fig. 6. Precision Fraction-
ating Column*

T, thermometers recording
temperatures of distilla-
tion and column jacket

P, tip of total reflux con-
denser where drops may
be counted

R, electric resistance heater

H, glass helices

flow into the receiver, is very important in problems of varying difficulty in fractionation. If the components are difficult to separate, the operator may divert into the receiver only 1 drop of liquid for every 20, 30, or even 50 sent back to the column. In cases of easy separation, a reflux ratio of five to one, or ten to one, would be satisfactory.

In some columns (for instance, Ref. 23, p. 44) the vapors from the column are only partially refluxed, and a small residual vapor fraction is sent to a condenser connected to a receiver. The principle is similar, but the mechanics of separating condensate from distillate differ.

STEAM DISTILLATION

43. If piped steam service is not available in the laboratory, a common gallon can or even a flask may be used as a boiler. It is convenient to silversolder a short piece of 5/16-inch copper tubing into a copper or brass washer with 5/16-inch hole. A hole is punched (not drilled) in the can with a large nail, and the copper device attached with soft solder. This copper fitting is readily shifted to a new can as the first wears or rusts out.

When such a boiler is employed it is essential to use the safety tube as shown in the illustration. This is simply a piece of 5 mm. glass tube 50 to 75 cm. in length. If placed in the position shown in the figure, it will give warning through escape of steam when the water level in the can falls below a safety line, set about 2 cm. above the bottom. Furthermore, the tube serves as protection in case the ordinary outlet from the apparatus should become obstructed.

The safety tube may also prevent still another misfortune. Should the flame under the can be extinguished accidentally during active steam distillation, there might be a vigorous suckback from the central flask. If, however, the central flask is set at a low position, as shown in the figure, and if furthermore the depth of water in the can is not too great, upon extinction of the flame air will be sucked through the safety tube and no harm done.

The substance to be steam-distilled is placed in the middle flask. By setting this flask at an angle one can prevent to a large extent the splashing of impure boiler liquid into the tube leading to the condenser.

The connecting tubes may well be of large (8 to 10 mm.) glass tubing. This size permits a more rapid passage of steam, and thus a more rapid distillation. Since the liquid is more actively stirred, a better yield ratio is attained. Moreover, the use of large connecting
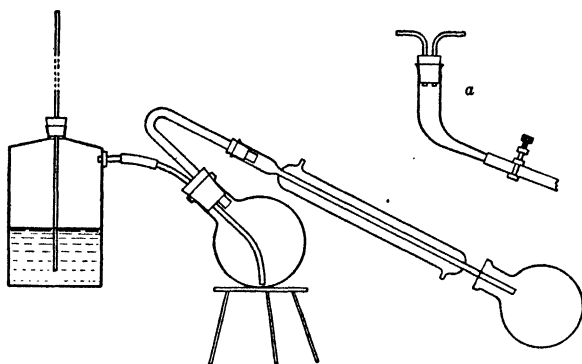
Apparatus for Steam Distillation

tubes makes it more difficult for liquid splashed from the impure mixture to be forced over into the receiver.

If piped steam service is furnished, use the adapter and screw clamp shown in *a* of the figure. This assembly serves as a water trap between the steam valve and the central flask.

For theory of steam distillation see § 83.

Questions

1. Why should the side stem of a distilling flask protrude from the cork which connects it with the condenser?

2. How would you distil a small quantity (*e.g.*, 10 g.) of a very stable substance whose boiling point is 300° C.?

3. Why should not the bulb of the thermometer be placed nearer to the level of the boiling liquid than the position shown in Fig. 2, § 33?

4. Why do we not use a Liebig condenser in ordinary reduced-pressure distillation? Under what conditions would such a condenser be preferable to the simple flask arrangement (§ 36, Fig. 1)?

5. Does it make any difference where the manometer is connected in a reduced-pressure distillation outfit? Why?

6. Why is it sometimes desirable to place a burner under the main or central flask in an outfit for steam distillation?

CHAPTER 6

Theory of Distillation

PURE SUBSTANCES

44. Vapor Pressure. The process of distillation consists mainly of two operations, namely, the transformation of a liquid into vapor, and the recondensation of that vapor in a separate section of the apparatus. If such a process is to be feasible, there must be a tendency of the molecules to escape from any exposed surface of the liquid and thus go into the gaseous state. This outward motion may be regarded as a bombardment of any surface or object within range. Such bombardment causes pressure on the surroundings, and thus the liquid is said to exert vapor pressure. In earlier literature the phenomenon was sometimes called "vapor tension."

If the substance exerting such pressure is not confined, it should eventually disappear; but if contained in a partly filled distilling flask, most of the departing molecules are compelled to remain in the vicinity. They collide with each other and with the walls of the flask, frequently rebounding into the liquid.

At any given temperature the escaping tendency, and thus the rate of escape of molecules per unit surface of the exposed liquid, is constant. The rate of return, however, grows with increasing concentration of the newly produced vapor. Soon the rate of return just equals the rate of escape, and equilibrium is attained. The pressure in the vapor phase becomes constant and is subject to measurement with a suitable gauge.

If the temperature is now elevated, the rate of escape rises, thus compelling a new and increased vapor concentration. Soon the rate of return again matches the rate of escape, and a new equilibrium is attained. The vapor pressure is greater than before. From experiments of this type thousands of numerical values of vapor pressure for various substances at various temperatures have been determined and recorded. Examples of these are seen in § 445.

While recorded in the literature simply as "vapor pressure," each of these numerical values refers to a vapor pressure at equilibrium and is usually expressed in millimeters of mercury.

45. Partial Pressure. If a liquid whose vapor pressure is less than 760 mm. is held in a partly filled but unstoppered flask, the space above the liquid is necessarily filled, not with pure vapor, but with a mixture of air and that vapor. If the vapor pressure happens to be 100 mm., 100/760 of the molecules in the upper space are of the given substance, and the residue of 660/760 is air. In this simple calculation the standard atmospheric pressure of 760 mm. is assumed. Heating of the system raises the vapor pressure and causes the molecules of vapor to replace those of air. In general, the variable fraction of the total gaseous pressure which is due to one particular species of molecule is called the **partial vapor pressure** of that component under the conditions at hand, without necessity of equilibrium.

Fig. 1. *Vapor Pressures of a Liquid*

Further increase in temperature eventually causes the vapor pressure to reach 760 mm. The partial vapor pressure becomes the whole pressure. The air is practically all displaced. Further heating will of course tend to elevate the pressure above 760 mm. Before the pressure exceeds 760 mm. by a measurable amount, however, the vapor will overcome the resistance of the external atmosphere and pour out of the flask.

Since the heating of such a vessel is usually done from below, the bottom of the flask will be the first part to reach the maximum temperature, that is, the point at which the vapor pressure is just about to exceed 760 mm. If now a bubble can be started, a sudden expansion of vapor will occur under the liquid surface. In other words, the liquid boils.

46. Boiling Point. Since a liquid is now being transformed into gas in relatively large quantity, heat (of vaporization) is absorbed
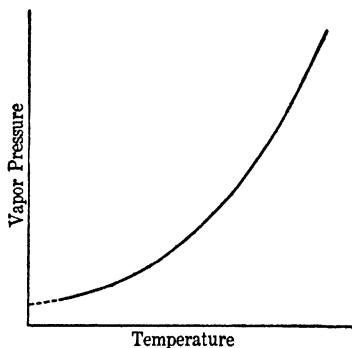
by the system in substantial amount. The temperature no longer rises. On the other hand, it cannot fall even the smallest amount, lest the vapor pressure fall and boiling stop at once. There is thus fixed a single definite temperature, to be known as the (normal) "boiling point" of the substance. If the preparation at hand is a pure substance and is chemically stable, there is no fundamental reason why the boiling point could not be determined with high precision, perhaps to the hundredth or thousandth of a degree. The boiling point is thus a valuable mark of distinction of the given substance. In the ordinary laboratory, however, one seldom troubles with such fractional precision. A determination accurate within one degree is usually adequate, unless one is making a special test of purity.

Unless otherwise specified, the boiling points of substances as reported in the literature are supposed to refer to standard pressure, 760 mm. Not all research workers have been careful, however, to observe abnormal barometer readings or record the fact that they worked in locations somewhat above sea level. Pressures other than 760 mm. should be recorded in parentheses after boiling-point figures.

47. Bumping. The process of boiling does not always proceed smoothly. The liquid "bumps," alternately ejecting excessive amounts of vapor—perhaps blowing spray into a condenser—and then lying for a time without ebullition. The presence of crystalline salts, and sometimes the existence of a peculiar colloidal condition, seem to be connected with the habit of bumping.

Whatever be the original cause of trouble, the immediate occasion is likely to be the lack of a supply of air or other gaseous material at the point from which the bubbles should be starting.

48. Remedies for Bumping; Boiling Stones. The introduction into a liquid of some inert object that will slowly emit small quantities of air normally solves the bumping problem. Scraps of platinum, bits of unglazed clay plate, fine capillary tubes closed at one end, carborundum crystal fragments, glass wool, and even anthracite coal have been used for this purpose. The platinum is useful by virtue of its well-known habit of absorbing large quantities of gases. The clay plate may also absorb air; it also certainly has numerous cavities in which air is merely occluded.

Each particle or potential bubble of air, emerging from the clay plate, exists at a pressure somewhere near 760 mm. Immediately the liquid, at 760 mm. vapor pressure itself, delivers vapor in relatively large quantity to the air bubble. The total pressure—air plus vapor—inside the bubble promptly rises above 760 mm. At once a rapid expansion occurs with the assistance of the ample heat supply close at hand. A vapor bubble is promptly expelled, and boiling proceeds quietly.

It is thus advisable to place boiling stones at the outset in vessels in which distillation is to be conducted. (See § 180 for details of preparation of the stones.) If a distillation is interrupted, it is advisable to add one or two new stones before the heating is resumed. Otherwise trouble may arise from the fact that the first supply of stones, partially freed from air by heating, will absorb liquid so thoroughly upon cooling that they no longer readily release the air still contained.in their innermost parts.

Beginners are warned at this point not to drop stones into a liquid which has already been heated to boiling without earlier provision of boiling stones. In such a case the liquid may already be at a temperature above its normal boiling point. A sudden outburst of vapor and spray may throw acid or flaming liquid upon the worker. When the operator realizes that he needs boiling stones, he should wait at least two minutes after the burner is removed before applying the remedy.

49. Heating Methods. Bumping may often be prevented, or at least reduced in violence, by the use of a heating bath instead of the simple system of burner and wire gauze. An oil bath or water bath permits many of the bubbles of vapor to rise from points around the edge of the liquid, and not all from the bottom of the flask. In reduced-pressure distillation this plan is particularly advised, and often absolutely necessary, even with the assistance of a capillary tube. If the bath temperature is near the temperature of the boiling liquid, danger of superheating is lessened, and consequently bumping is diminished.

50. Prevention of Bumping by Evolution of Hydrogen. If an aqueous reaction mixture is either faintly alkaline or faintly acidic, the addition of one or two pieces of zinc often gives protection from bumping. The liquid reacts very slowly with the zinc, yielding

minute hydrogen bubbles and thus permitting smooth ebullition. Naturally such a method is employed only if the addition of a small amount of zinc salts is not harmful.

51. Use of a Condenser. When a liquid of boiling point below 150° C. is distilled, the vapors are led into a condenser (Liebig or similar type) through which water may circulate. Some workers advise filling the condenser with water and shutting off the steam before actual distillation if the liquid boils between 120° and 150°. If the liquid boils below 120°, the water is allowed to circulate.

On the other hand, if the liquid boils above 150°, the water jacket is not only unnecessary, but introduces the hazard of cracking of glass. A simple air-cooled tube replaces the Liebig condenser. If the temperature of a single distillation varies over a wide range from values far below 150° to those above 150°, the water-cooled condenser would ordinarily be exchanged for one of air-cooled type as the higher figures were approached. Where such an exchange is inconvenient, a water-cooled condenser with inner tube of Pyrex glass is used for the whole operation, with reduced hazard of breakage.

DISTILLATION UNDER REDUCED PRESSURE

52. Capric Acid. Examination of the accompanying vapor pressure-temperature diagram for capric acid ($C_9H_{19}COOH$) shows that the boiling point of the substance may be substantially lowered by operation at pressures under 40 mm., a process readily carried out with simple apparatus. It happens that capric acid decomposes somewhat at 268°, its normal boiling point. A reduction of pressure to 20 mm., accomplished with the aid of a common water pump, permits distillation at 165°, a temperature so low that the substance is recovered with little or no decomposition.

Fig. 2. *Vapor Pressures of Capric Acid*

53. Calculation of Boiling Point. It is often impossible to find in the literature the boiling point of a substance at some particular reduced pressure which happens to be of interest. For example, vapor-pressure data for methylene bromide seem to be missing be-
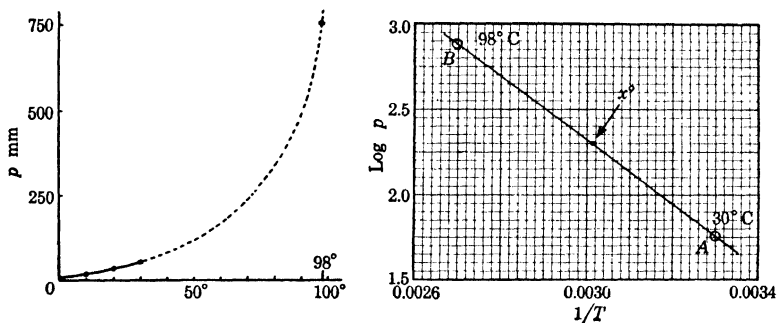
Figs. 3 & 4. Vapor-Pressure Curves of Methylene Bromide

tween 30° (56.4 mm.) and 98° (760 mm.), as suggested by the dotted portion of the curve in Fig. 3. Suppose one wishes to know the boiling point at 200 mm. Simple interpolation between 30° and 98° is not at all accurate, since the dotted line is decidedly curved and was only sketched in as a rough estimate.

An ideal solution of the above problem could be reached if one knew the equation of the vapor-pressure-temperature curve. This equation has the general form

$$\log p = \frac{-A}{T} + B,$$

in which p is the vapor pressure, T the temperature on the absolute scale, while A and B are special constants.

If now the values for p and T are substituted in the above equation for both 30° and 98° respectively, two simultaneous equations are obtained. From these equations the special numerical values of A and B pertaining to methylene bromide are available. As soon as A and B are known, solution for any new value of p, such as 200 mm., may be obtained. Most chemists, however, prefer to use this principle in a graphic method.

If log p is plotted against the reciprocal of T it follows from the above equation that a straight line is obtained. This gives a convenient solution to the problem at hand. Only two temperatures and the two corresponding pressures are needed to fix the position of the straight line, as shown in AB of Fig. 4.

In the present example (Fig. 4) A is the plot of log 56.4 against the reciprocal of 303° (30° C.), and B of log 760 against the reciprocal of 371° (98° C.). After the straight line is drawn through points A and B, one need only locate the point X on that line at the level corresponding to log 200. The corresponding temperature is then readily derived from the horizontal or abscissa reading of X, and proves to be 324° A, or 51° C. In like manner temperature values could be obtained by extrapolation below A or above B in Fig. 4, but such should not be carried to extremes either of low or high pressure. Within reasonable limits the method is fairly accurate.

54. Abnormal Barometric Pressure. If the laboratory is located at a high altitude, or is operating under abnormal weather conditions, the standard normal boiling points will require correction even in common distillation. This should be readily accomplished by the graphic method described in § 53; but unfortunately only one boiling-point value (that at 760 mm.) is known for each of many cases, and the logarithmic graph is impossible.

If the elevation is not over 1000 feet, and thus the deficiency in atmospheric pressure not likely to exceed 35 mm., a rough calculation of the boiling-point correction (Δt) may be made according to Craft's rule,

$$\Delta t = 0.0001 \ \Delta p \ T_B,$$

where Δp is the deviation (up or down) of the barometer from normal, in millimeters, and T_B is the normal boiling point on the absolute temperature scale, at 760 mm.

Example. What is the boiling point of n-heptane at 730 mm. pressure?

This substance boils at 98.5° C. at 760 mm. pressure.

$$\Delta t = 0.0001 \times 30 \times 371.5° = 1.1°$$

Therefore the boiling point at 730 mm. is 98.5 − 1.1 = 97.4° C.

It must be frankly conceded that Craft's rule is only a rough ap-

proximation which does not take into account the possibility of an "associated" liquid. In regions of extreme barometric deficiency, as in the Rocky Mountain belt, it is necessary to use more precise and thus more complex equations. Information as to these methods may be found in recent editions of the handbooks of chemistry, particularly those of Hodgman (Chemical Rubber Company) and of Lange.

55. The Problem of Bumping. Any possible trouble from bumping is likely to be aggravated if the pressure of the distillation is greatly reduced. For example, distillation at 20 mm. often is decidedly less smooth than ordinary distillation at 760 mm. An increase from the 20-mm. value even to 40 or 50 mm. is likely to be very helpful. A consideration of the change in volume of a liquid evaporated at 20 mm., in contrast to the change at 100 or 760 mm., throws light on this situation. For example:

Suppose the capric acid cited in § 52 is distilled at 760 mm. A simple calculation shows that each cubic millimeter of the liquid, arbitrarily taken as a portion being distilled at a given moment, expands about 250-fold when it goes into the vapor state, producing 0.25 cc. of vapor. This 0.25 cc., appearing at the bottom of the distilling flask, naturally forms a bubble of moderate size which rises and escapes without great disturbance.

Let this experiment be now repeated at 20 mm. The 1 cu. mm. portion of liquid now evaporates at a much lower temperature. This factor alone would, to be sure, tend to reduce the size of the bubble about to be produced. At 20 mm., however, a great expansion is necessitated by simple "Boyle's law" effect. The small portion becomes about 8 cc.—roughly an 8000-fold increase in volume. So great an expansion tends to cause violent ebullition, excessive splashing, and bumping.

To minimize these difficulties the two-necked Claisen flask offers some assistance. In such a flask (see § 35) it is relatively difficult for splashings of liquid to be carried mechanically to the side stem.

Of equal importance to the bumping problem is the choice of heating methods. Direct heating of a reduced-pressure flask, applied under wire gauze from a common Bunsen flame, is to be avoided. Such heating encourages the oversize bubbles to be formed at a low level, where they tend to lift the whole mass of liquid out of the boiler. As these bubbles rise, they are relieved of

hydrostatic pressure and thus tend to burst out with accelerated violence. Such relief of pressure would not be of any relative importance in a distillation at 760 mm.; but at low pressures the difference in pressure between top and bottom of a liquid is of significance. In distillations at extremely low pressures, such as 0.01 or 0.001 mm., the very weight of liquid in a flask would be more than enough to counteract the upward pressure of a potential bubble. In such cases, accordingly, no bubbling is expected, and the operation really becomes a low-pressure evaporation.

The Claisen flask is therefore immersed in a heating bath—using water where the boiling point (under reduced pressure) does not exceed 100°, and oil for higher temperatures. Much of the evaporation in such a case occurs around the edge of the liquid. Furthermore, the use of the oil bath with distillations at high temperatures eliminates the risk of overheating a flask at one point and reduces the danger of violent collapse of the vessel with possible injury to the operator. A distilling flask should be examined carefully for cracks before mounting in an oil bath. Occasionally a Pyrex flask, carelessly handled, strikes some hard pointed object, which makes a tiny fractured spot with radiating cracks. Such a flask, being of specially good glass, may not fail under ordinary treatment, and the flaw may not be noticed. Under reduced pressure, however, an accident is possible.

56. Errors in Pressure Readings. A careful worker is expected to report as accurately as possible the pressure at which a given substance was distilled. In ordinary distillation an error of 2 or 3 mm. in the measurement of pressure is of no great significance. For example, at 757 mm. the boiling point of an organic compound may be only one or two tenths of a degree below the standard figure for 760 mm. At reduced pressure, however, the vapor-pressure curve is much flatter, and a change of 2 mm. may make a great difference in boiling point. Of course such differences are obvious and easily determinable if one has a good pressure gauge in connection with the apparatus; but there is still opportunity for deceptive error if the capillary tube in the Claisen flask is too large.

Suppose a distillation is being conducted in apparatus where the pressure gauge, or manometer, reads 10 mm. It happens that the bore of the capillary in the Claisen flask is too large, admitting far too much air. The vapor passing from the flask to the condenser is not

pure, but contains perhaps 10% of air. The partial pressure of the air inside the flask is 2 mm. The partial pressure of the organic vapor is accordingly 10 less 2, or 8 mm. The liquid under these conditions will "boil," not at the temperature appropriate to 10 mm., but at the very different temperature for 8 mm. Not only are the resulting numerical data erroneous, but the excess of air may sweep unduly large quantities of product entirely through the apparatus. The air may also tend to oxidize the hot organic vapors to an excessive degree, though not necessarily with visible result.

DISTILLATION OF MIXTURES

57. Nonvolatile Impurities. Suppose that pure water, boiling normally at 100° C. (760 mm.) is treated with a nonvolatile, but soluble substance like sugar. From the resulting sugar solution it will be more difficult for water vapor to escape. Accordingly the vapor pressure will fall short of 760 mm. A higher temperature will be necessary in order that the solution may boil. This phenomenon, like several other important relations to be discussed in succeeding chapters, is governed by Raoult's law:

The partial vapor pressure of a component in a solution varies directly with its mole fraction.

58. Mole Percentage. In discussions of the applications of Raoult's law it is customary to speak of mole percentage, or mole fraction, as contrasted with ordinary percentage values, which refer directly to weight. For example, a mixture of 180 g. of acetic acid (mol. wt. 60) and 90 g. of water (mol. wt. 18) obviously contains 180/270, or 66.7%, of acid and 90/270, or 33.3%, water. These figures are for ordinary "weight per cent." But 180 g. of acetic acid is 3 moles, while 90 g. of water is 5 moles, total 8 moles. Three-eighths of the moles, or 37.5 mole per cent of the mixture, is acetic acid, while the remainder, 62.5 mole per cent, is water.

In all subsequent discussion, however, including directions for experiments, any percentage value means "percentage by weight" unless otherwise specified.

59. Raoult's Law. The following example illustrates Raoult's law applied to solutions of a nonvolatile substance.

Suppose 1000 moles of water at its normal boiling point (100°,

760 mm.) is taken for an experiment. One mole of this quantity is now replaced with 342 g., or 1 mole, of sugar. The fraction of solvent is reduced exactly 0.1 mole per cent, or to 99.9 mole per cent of its former value.

As Raoult's law would predict, and as actual experiment shows, the vapor pressure of the liquid falls to 99.9% of its former value; that is, from 760 mm. to 759.24 mm. Increase of the fraction of sugar to 0.2 mole per cent (2 moles of sugar to 998 moles of water) lowers the aqueous vapor pressure to 99.8% of 760, or 758.48 mm., and so on.

Such regularity of behavior occurs in almost any solution containing very low concentrations of the nonvolatile impurity. With more concentrated solutions substantial deviations from the rule appear, depending on the kind of impurity present.

A regular fall in vapor pressure, as above described, naturally suggests an equally regular rise in boiling point as the mole fraction of water is decreased. Thus in very dilute solutions the boiling point of water rises at the rate of about 0.3° per mole per cent of solute, or 0.53° for 1 mole in 1000 g. of water. This observation suggests the well-known method of determining molecular weight by elevation of boiling point.

The careful worker in organic chemistry will therefore be on his guard against recording a boiling point if the boiling liquid may contain dissolved impurities. It is possible, however, to determine the boiling point of such a substance by the method of **recondensation.** The liquid, in which any impurities are of nonvolatile type only, is boiled in a flask with a long neck. A thermometer is mounted with the mercury bulb up in the neck at some distance from the boiling material. As the solution boils, vapor may be emitted at an elevated temperature, in agreement with Raoult's law; but in passing up through the neck of the flask it is cooled to its true boiling point if the distillation is conducted at a moderate rate. Part of the vapor now recondenses and flows down over the lower part of the thermometer. Under such conditions, the thermometer, if accurately calibrated and completely immersed in condensing vapor, will show the true boiling point. (See § 186.)

60. Mixture of Two Liquid Substances. Miscible Liquids. A mixture of two similar liquid substances which do not react with each other is often called an "ideal solution," and obeys Raoult's

law rather closely. A mixture of *n*-pentane and *n*-heptane, two inert hydrocarbons of like character, is an example. Knowledge of the vapor pressures of these substances at different temperatures will make it possible to predict the behavior of various mixtures during distillation.

Problems. The use of these numerical values is illustrated in the following problems.
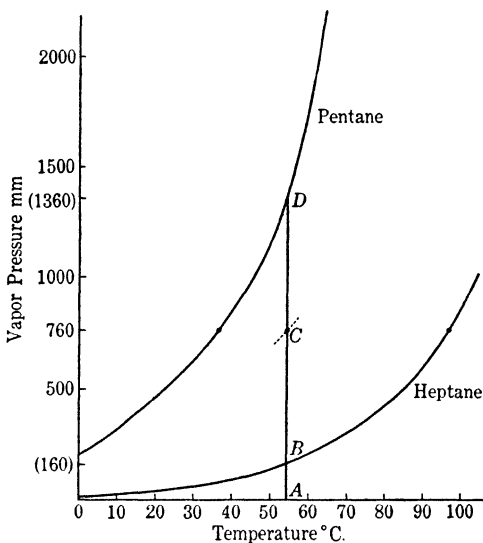
Fig. 5.   Vapor Pressures

(1)   What is the vapor pressure of a mixture of 108 g. of *n*-pentane and 50 g. of *n*-heptane at room temperature (20° C.)?

$$108 \text{ g. of pentane (mol. wt. } 72) = 1.5 \text{ moles}$$
$$50 \text{ g. of heptane (mol. wt. } 100) = 0.5 \text{ mole}$$
$$\overline{\text{Mixture} \qquad\qquad 2.0 \text{ moles}}$$

According to Raoult's law the partial vapor pressure of pentane in the mixture will be 1.5/2.0, or 75% of the vapor pressure of pure pentane at 20°, since 75% of the molecules are of that species. Similarly the partial vapor pressure of heptane will be 0.5/2.0, or 25% of the corresponding value for pure heptane. (See tabular data in § 445.)

0.75 × 420 mm. = 315 mm.
0.25 × 36 mm. =   9 mm.

V.p. of mixture = 324 mm.

(2) What is the boiling point of a mixture of 36 g. of *n*-pentane and 150 g. of *n*-heptane in a laboratory where the barometer reading is 756 mm.?

In the absence of adequate data for the equations (§ 53) of the vapor-pressure curves, trick methods are called into service. This particular problem is readily solved by a cut-and-try method, since the desired boiling point happens to be one of the temperature values in the vapor-pressure table of § 445.

First the mole fraction (or mole per cent if one prefers) is calculated; in this case 1/4 pentane, 3/4 heptane. According to Raoult's law,

1/4 p_1 (pentane) + 3/4 p_2 (heptane) must equal 756 mm.

A rapid survey of the vapor-pressure table, with one or two possible wrong guesses, suggests that the values at 70° are promising, and these values are accordingly tested:

1/4 (2119) + 3/4 (302) = 756.25

This result, 756.25, is so close to the 756 mm. specified in the problem that one may immediately conclude, with negligible error, that the boiling point of the mixture in question is 70°. Such a neat coincidence is rare. More often the desired result is not a simple multiple of 10, and thus cannot be spotted directly in the customary table given in 10-degree intervals. One then resorts to the method of plotting on cross-sectional paper, as in problem (3).

(3) What is the normal boiling point of a mixture of 144 g. of pentane and 200 g. of heptane?

The vapor pressures of this mixture are calculated by the method of Prob. 1 for several 10-degree intervals in the region where the boiling point is expected. As soon as two or more values next above 760 mm., and two or more below 760 mm. are found, the vapor-pressure curve in the region of interest is plotted, as in Fig. 6. In this case the temperatures 40°, 50°, 60°, and 70° are plotted against 483, 667, 907, and 1211 mm. respectively. Since the known values are near by, the logarithmic method (§ 53) is unnecessary. A

smooth curve through the four points, marked in Fig. 6 by small circles, shows an intersection with the horizontal line for 760 mm. at 54°. The boiling point is therefore 54°, as marked at C in Fig. 5.

Finally, if one should take the trouble to draw Fig. 5 in full detail for each degree of tempera-ture, the values 1360 (line AD) and 160 (line AB) would be found for pen-tane and heptane, respec-tively, at 54°. This gives a chance to test the graphic solution above reported:

$$(1/2 \times 1360) + (1/2 \times 160) = 760 \text{ mm.}$$

(4) What mixture of pentane and heptane will boil at 60°?
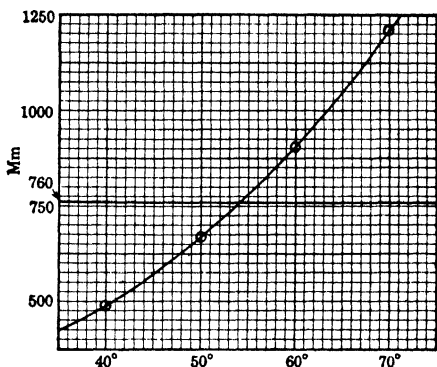
Fig 6. Determination of Boiling Point

Let x = the mole per cent of pentane, and
$100 - x$ = the mole per cent of heptane.

According to data from § 445, and Raoult's law, the partial vapor pressure of pentane will be $x\%$ of 1605 mm., the vapor pressure of pure pentane at 60°. Similarly, the partial pressure of heptane will be $(100 - x)\%$ of 209 mm. The sum of these partial pressures must be 760 mm. if the mixture is to be at its boiling point.

$$\left(\frac{x}{100} \times 1605\right) + \left(\frac{100 - x}{100} \times 209\right) = 760$$
$$x = 39.5 \text{ (mole per cent pentane)}$$
$$100 - x = 60.5 \text{ (mole per cent heptane)}$$

If the proportions by weight are desired, it is convenient to calcu-late the weight of a total of 100 moles of the mixture:

39.5 moles $\times$ 72 (mol. wt. pentane) = 2844 g. pentane
60.5 moles $\times$ 100 (mol. wt. heptane) = 6050 g. heptane

100   moles of mixture   = 8894 g.

It is evident from Fig. 5 that the boiling point of a 50 mole per cent mixture lies closer to the boiling point of pentane than its mere

mole fraction would suggest. In cases where the boiling points of the two components are still farther apart, the tendency of the boiling point of a mixture to be relatively low is more noticeable.

This behavior in part explains the fact that ether (b.pt. 35°) is easily separated from aniline (b.pt. 184°) by distillation.

61. In Fig. 7 are plotted the boiling points of all possible mixtures of pentane and heptane. The continuous line of the graph marks
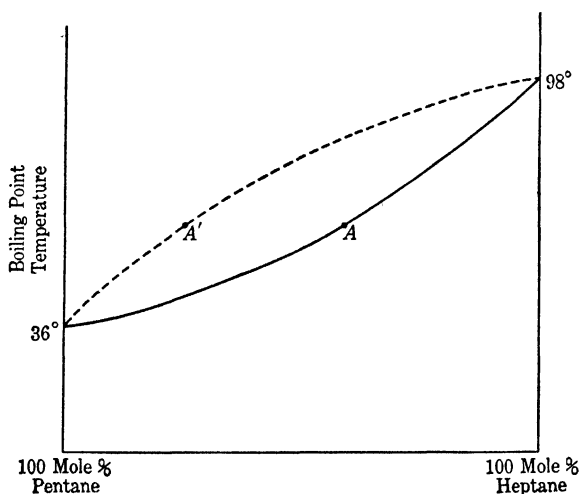
Fig. 7.   Boiling Point—Composition Diagram

the boiling point for every possible composition. The dotted line marks the composition of the particular vapor which comes by simple distillation of each liquid mixture. For example, the mixture of 39.5 moles of pentane and 60.5 moles of heptane, described on a previous page, is marked as A, boiling at 60°. The vapor which comes from a distillation of A, rich in the more volatile component pentane, has the composition A', and this new point is set on the same horizontal level as A, since A' has the same temperature as A. The question at once arises—How far to the left of A will A' be located; or in other words, what is the composition of the vapor A'? Of course the answer to this question may be obtained by experiment. The vapor A' may actually be analyzed chemically. It is simpler, however, to use Raoult's law:

39.5% of 1605 mm. = 634 mm., the partial pressure of pentane in the liquid being distilled.

60.5% of 209 mm. = 126 mm., the partial pressure of heptane in this liquid.

Since the vapor A' must be at equilibrium with the liquid A, the pressures of the two components in the vapor phase are also 634 and 126 mm. respectively. But Avogadro's law states that the partial pressures of the components in a mixture of gases measure the relative numbers of molecules of each species, respectively, in unit volume of the mixture. A simple illustration is seen in dry air at sea level (760 mm.). The partial pressure of oxygen in such air is approximately 0.21 atmosphere, or about 159 mm.; of nitrogen, 0.78 atmosphere, or about 593 mm.; of minor constituents, 0.01 atmosphere, or about 8 mm. Therefore air contains 21 molecules of oxygen for each 78 of nitrogen; or 159 oxygen to 593 nitrogen.

Similarly the vapor A' will contain 634 molecules of pentane for every 126 molecules of heptane, total 760 molecules. Dividing 634 by 760, one determines the mole percentage of pentane, which is 83.4, and thus locates the position of A' with respect to the composition axis.

62. Change during Distillation. It is clear that a vapor of which 83.4 mole per cent is pentane cannot be withdrawn from a liquid containing only 39.5 mole per cent pentane without immediate disturbance of the conditions initially present in the boiler. With loss of pentane the boiling point rises, and the distillate becomes increasingly richer in heptane; but the distillate being produced at any given moment is always richer in pentane than the boiler liquid existing just at that moment. The temperature, at first just 60°, rises steadily, and approaches 98° as the boiler goes dry.

Two practical conclusions may be drawn at once. First, a rising temperature of boiling means that *at least two* substances are present. That is, the liquid is certainly not a pure substance—or if originally pure, it has decomposed at least partially. Second, a "straight" distillation does not give a satisfactory separation of two components. Two improvements of method are possible; (*a*) to distil repeatedly into a succession of receivers, as described in § 73, or (*b*) to employ a fractionating column (§ 74).

63. Fall in Temperature. Students frequently report that the boiling temperature of a liquid fell at some time during distillation. No such phenomenon as a drop in boiling point is recognized in properly conducted distillation. The worker must have permitted the flame to be blown aside by a draft, or in some other way he allowed the flask to become cool, with resulting backflow of cool air from the condenser. The fall in temperature thus has no significance in the distillation other than an indication of faulty technique.

64. Deviations from Raoult's Law. Many liquid mixtures do not obey Raoult's law. In some cases the vapor pressures are greater than those calculated from tables and mole fractions. A **positive deviation** from the law is then recognized. In other cases the vapor pressures are abnormally low, indicating a **negative deviation.** An example of each of these will be discussed.

65. Positive Deviation. Whenever two liquids, though miscible and mutually nonreactive, are quite different in fundamental makeup, a positive deviation often occurs. Apparently the two liquids have an abnormally great tendency to escape from one another. Were that tendency greater, they might part into two liquid phases like ether and water. Under certain conditions, however, they actually stay together as a single liquid phase, but manifest their mutual "dislike" of each other by exerting abnormally high combined vapor pressures in mixtures.

Since these mixtures tend to have high vapor pressures, they have correspondingly low boiling points. So great is the depression of boiling point that in certain ranges of composition the mixture may boil at temperatures even below the boiling point of the more volatile of the two components.

66. The system ethyl alcohol-water is the best known case of positive deviation. At one composition (95.57%) aqueous ethyl alcohol boils at a temperature below the boiling point of pure ethyl alcohol. For convenience in oral explanation, this value is rounded off to "96%" in the following paragraphs.

Figure 8 shows the boiling point of 96% alcohol to be only 0.15° below the boiling point of pure alcohol; nevertheless this small difference is enough to make considerable trouble in both the industrial and laboratory processes of preparing pure ethyl alcohol. The phenomenon makes it impossible to produce pure ("absolute")

alcohol by any kind of fractional distillation of mixtures of alcohol and water alone. It may be noted that commercial ethyl alcohol is seldom of so high a percentage as 96%, but commonly contains a slightly greater content of water.

In Fig. 8 it is seen that aqueous alcohol of 50% composition (*A*) will yield a distillate (*A'*) richer in alcohol—just as one would expect
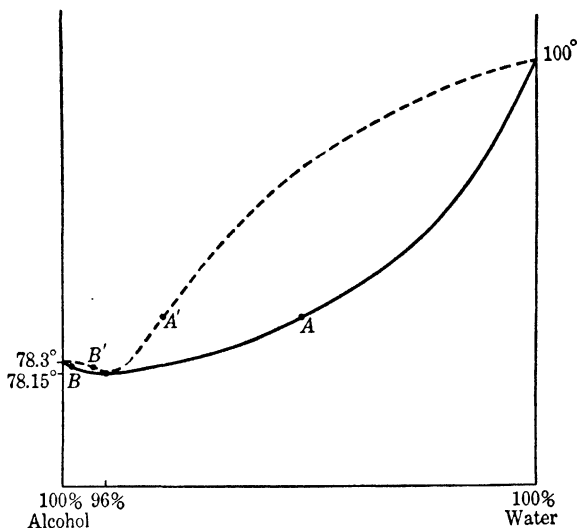
Fig. 8. Boiling Point—Composition Diagram for Ethyl Alcohol and Water

in a case where Raoult's law was obeyed. On the other hand, 99% alcohol (*B*) yields a distillate (*B'*) richer in water—richer in the *less volatile* component. If 96% alcohol is distilled, vapor of exactly the same (96%) composition comes over. The boiler contents do not change. Evidently therefore the entire quantity of liquid could be distilled without change in temperature or composition. Such a mixture is commonly called a "constant boiling mixture," "azeotropic mixture," or, when composed of just two substances, a "binary mixture."

An azeotropic mixture may easily deceive an original investigator into thinking he is dealing with a pure substance. Unfortunately there are many such mixtures known. Most of these are of the minimum-boiling type above described, and a few of maximum

boiling point as described in § 68 below. Distillation engineers must be constantly on their guard in the operation of processes involving mixtures of solvents.

67. Repeated Distillation of Aqueous Alcohol. The repeated partial distillation of any mixture of alcohol and water will eventually yield a distillate of the azeotropic composition. It is assumed that a certain residue is set aside, or discarded, each time from the distilling flask. For example, a fermented fruit juice, containing 5% of alcohol, upon simple distillation might yield a 20 or 25% solution of alcohol, there being a substantial rejection of aqueous boiler residue, or "slop" as the distiller calls it. Repeated redistillations, with successive rejections, will gradually raise the percentage to 96%, but not higher. If a fractionating column is included in the apparatus this advance from 5 to 96% may be made in fewer steps—in two distillations, or perhaps even in one operation. Again there is no possibility of getting above the 96% mark.

Where really pure alcohol is desired, one may employ chemical means, usually with the aid of quicklime, as explained in § 212. Industrially the result is accomplished much more expeditely by the introduction of a third solvent, benzene, into the aqueous alcohol. When the three-component mixture is distilled through proper fractionating apparatus, a "ternary" azeotropic mixture of the three substances passes over until the water is exhausted. A second azeotropic mixture, this time of benzene and some alcohol, then goes over until the benzene is practically exhausted. Further distillation yields absolute alcohol.

68. Negative Deviation. Sometimes the sum of the partial vapor pressures of two components is abnormally low, illustrating negative deviation from Raoult's law. The boiling-point curve will run high instead of low. In the case pictured in Fig. 9 there is a constant-boiling mixture of 20% acetone and 80% chloroform.

Distillation of an acetone-chloroform mixture will proceed in a manner contrary to that with alcohol and water. Any mixture of the two components, when boiled, will itself gradually become more and more like the azeotropic mixture. Either acetone or chloroform, as the case may demand, escapes in relatively large proportion, leaving a boiler residue which finally attains the composition of 20–80.

Relatively few of the high-boiling types of azeotropic mixtures are known in the field of organic chemistry.   This fact is probably related to the ordinary cause for negative deviation.   Usually the two components in such a case combine chemically to a certain extent, forming a relatively nonvolatile compound.   Naturally the residual
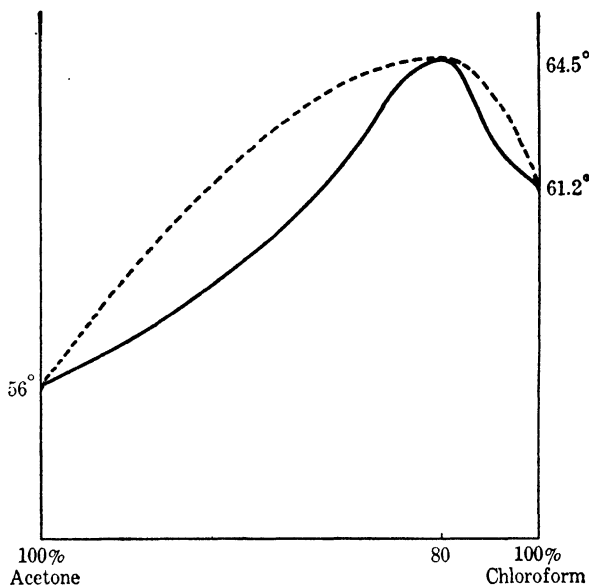
Fig. 9.   Negative Deviation

free component materials, present actually in reduced mole fraction, exert low partial vapor pressures.   Accordingly, the boiling points are high.

69. Several common inorganic acids, when mixed with water, yield high-boiling azeotropic solutions.   The 20.2% solution of hydr⌒chloric acid is a noteworthy example.   So faithfully does this reagent change to the 20.2% value that a standard solution of the acid may be prepared with a high degree of precision merely by distilling any aqueous solution of the acid until the boiler residue, and thus the current distillate, are of constant, and thus of azeotropic composition.   Arrival at the 20.2% point is expedited by starting with a solution of nearly that concentration, preferably above 20.2 rather than below.   Similarly, commercial "concentrated" nitric

acid is approximately a 68% azeotropic solution of nitric acid in water.   Hydrobromic and hydriodic acids have analogous behavior.
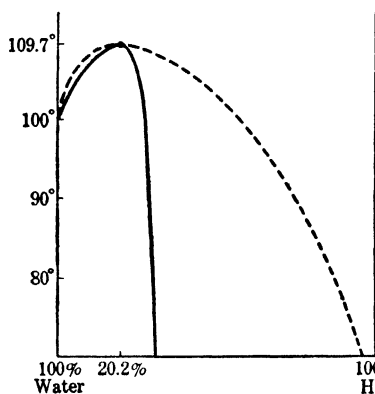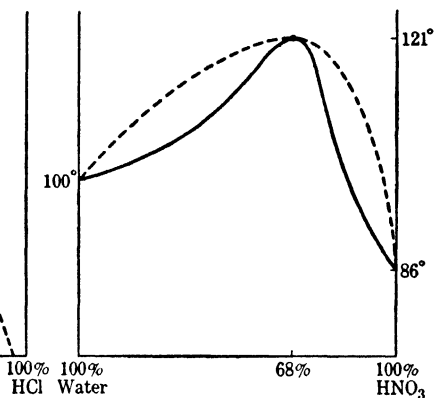
Fig. 10   Fig. 11

Boiling-Point—Composition Diagrams

70. The following are a few examples of the many known constant-boiling mixtures.   Information on others may be obtained from Robinson, *Fractional Distillation*, and *International Critical Tables*, Vol. 3, p. 318 (McGraw-Hill, New York).

MIXTURES OF MINIMUM BOILING POINT

Components	B.Pt.	Comp.	Constant B.Pt.
Benzene	80.6°	68%	68.25°
Ethyl alcohol	78.3°	32	
Benzene	80.6°	55%	77.5°
Cyclohexane	80.8°	45	
Carbon tetrachloride	77°	79%	55.7°
Methyl alcohol	65°	21	
Ethyl acetate	77°	69%	71°
Ethyl alcohol	78.3°	31	
n-Propyl alcohol	98°	53%	91°
Toluene	111°	47	

MIXTURES OF MAXIMUM BOILING POINT

Components	B.Pt.	Comp.	Constant B.Pt.
Chloroform	61.2°	22%⎫	64.5°
Methyl acetate	57.1°	78 ⎭	
Formic acid	101°	77%⎫	107.1°
Water	100°	23 ⎭	
Methyl ether	−23.7°	39%⎫	−2°
Hydrogen chloride	−83.7°	61 ⎭	
Phenol	181.5°	42%⎫	186.22°
Aniline	184.4°	58 ⎭	

DEVIATIONS FROM RAOULT'S LAW IN VERY DILUTE SOLUTIONS

71. Duclaux Constants. In the experiment on "Identification of an Acid" (see § 262) an aliphatic acid is identified virtually by measurement of the rate at which it escapes from a very dilute (2%) solution when the latter is distilled. One hundred cubic centimeters of the dilute solution is used; and the percentages of the total quantity of acid which pass over in the first, second, and third 10 cc. of distillate, respectively, are estimated. These percentages are known as "Duclaux constants." Some acids escape relatively rapidly and thus have large constants; others seem to be less active and have low constants.

DUCLAUX CONSTANTS

Acid and B.Pt.	First 10 cc.	Second 10 cc.	Third 10 cc.
Formic (101°)	3.95	4.40	4.55
Acetic (118°)	6.8	7.1	7.4
Propionic (141°)	11.9	11.7	11.3
n-Butyric (164°)	17.9	16.9	14.6
n-Valeric (187°)	24.5	20.6	17.0
iso-Butyric (155°)	26.0	20.9	16.0
iso-Valeric (177°)	28.7	23.1	16.8
n-Caproic (202°)	33.0	24.0	19.0

Strict adherence to Raoult's law would of course require that water, which is more volatile than any of the acids in question, should pass over in a distillation of dilute acid proportionately faster than the acid. The first 10 cc. of distillate would therefore contain more than 10% of the water originally present in the system and thus less than 10% of the acid. The case of acetic acid at least approximately complies with this presumption, since only 6.8% of the acid component is distilled in the first 10 cc.

The behavior of *n*-butyric acid is strikingly different. Since the Duclaux constant is above 10, it follows that a dilute solution of butyric acid, upon distillation, would yield a distillate *enriched in the less volatile* component. When such information, obtained from distillations at different concentrations, is plotted on a conventional boiling point-composition diagram, it necessarily follows that butyric acid and water exhibit at some point the phenomenon of azeotropic *minimum* boiling point, of the type illustrated in Fig. 8, § 66. The high Duclaux constant (17.9) is thus seen to be the direct result of a marked positive deviation from Raoult's law.

Formic acid, on the contrary, has an exceptionally low constant, despite the fact that it is the most volatile acid. In this case, however, it is likely that an unusually large proportion of the acid is held back as a less volatile hydrate. A negative deviation results, with low vapor pressures, and a maximum azeotropic boiling point of the type described in § 68.

72. Irregularities. Caproic acid, with a large Duclaux constant, would undoubtedly form a minimum-boiling azeotropic mixture if its solubility in water were sufficiently great. Actually the acid is not miscible with water in all proportions, so that the zone of simple one-phase azeotropic mixtures happens to be excluded. In such a case the process of Duclaux distillation approaches in physico-chemical character a normal steam distillation, in which two dissimilar components escape rather independently.

The above discussion of course is primarily intended to throw light on the particular analytical method under discussion; but it has other applications. Laboratory workers frequently have occasion to prepare a volatile organic compound in a dilute reaction mixture, and naturally attempt to isolate the desired substance from the water by fractional distillation. A consideration of these principles

may show whether the principal yield of the substance is to be expected in the early fractions, or the late ones—quite aside from the boiling point of the pure substance itself.

References on Distillation

Alexander Findlay, *The Phase Rule* (Longmans, New York).

Clark S. Robinson, *Fractional Distillation* (McGraw-Hill, New York).

Sidney Young, *Distillation Principles and Processes* (Macmillan, New York).

P. N. Evans, *Ind. Eng. Chem.* **8,** 260 (1916).   A discussion of alcohol-water mixtures.

W. J. Podbielniak, *Ind. Eng. Chem. Anal. Ed.* **13,** 639 (1941).   Precision apparatus for fractionation.

Problems of Distillation

(See § 445, on vapor pressures, and § 70, on azeotropic mixtures, for necessary data.)

1. What is the vapor pressure of a mixture of 7.2 g. of *n*-pentane, 20 g. of *n*-heptane, and 22.8 g. of *n*-octane at 20°?

2. What is the boiling point of a 40 mole per cent solution of *n*-octane in *n*-pentane at the elevation of 1000 feet above sea level, where the barometer reading may be taken as 735 mm.?

3. If a mixture of 1 mole of bromobenzene and 2 moles of *p*-dibromobenzene were distilled under reduced pressure at 100°,

(*a*) What would be the pressure in the distilling flask?

(*b*) What would be the mole fraction of bromobenzene in the first drop of distillate which came over?

(*c*) What would be the percentage composition (by weight) of the first drop so collected?

(*d*) In a general way, what change would take place in the composition of the residual liquid in the distilling flask as the distillation proceeded?

4. Assuming the validity of Raoult's law, what mixture of *n*-octane and bromobenzene boils at 30° and 16 mm. pressure?

5. Calculate (*a*) the mole fraction of *n*-octane in that mixture of *n*-octane and *n*-heptane which boils at 100°, and (*b*) the weight percentage of *n*-octane in the first vapor coming from this boiling mixture.

6. What is the vapor pressure of methylene bromide at 77° C.?   (See Fig. 4, § 53.)

Deviations from Raoult's Law

7. Suppose a solution of 10 g. of phenol in 90 g. of aniline were completely distilled. Describe in a general way, without exact calculation, how the composition of the succeeding drops of distillate would change during the entire process.

8. A mixture of equal weights of benzene and cyclohexane is completely distilled from a simple boiler without a fractionating column or equivalent.

(*a*) In what way would the composition of the first few cubic centimeters of distillate differ from that of the original mixture?

(*b*) How would the last few cubic centimeters differ from the original mixture?

9. Suppose a solution of 10 g. of formic acid in 90 g. of water were distilled until just 50 g. of distillate had been collected. In which vessel would the larger part of the formic acid be, the boiler or receiver, at this point?

Molecular Weight Relations

10. A 2% solution of glucose in water boils at 100.06°. What would be the boiling point of a 5% solution of glycerol?

11. What is the molecular weight of a substance if a solution of 30 g. of the compound in 1 l. of water boils at 100.4°?

12. Suppose a pure liquid compound should start to polymerize. What effect on the boiling point of the liquid might be expected? Why?

CHAPTER 7

Theory of Fractional and Steam Distillation

FRACTIONAL DISTILLATION

73. Distribution into Multiple Receivers. Simple distillation of a mixture of two liquids normally yields at first a fraction rich in the volatile component, at the end a fraction rich in the less volatile component. Repetition of such a distillation, into multiple receivers, effects a sharper separation. In such a process various distillates are poured back at intervals into the boiler and redistilled. The actual scheme of performance is too complicated to permit an intelligible explanation in general terms. It is perhaps better to outline the procedure concretely in an imaginary case, supplying plausible data to show the progress of the separation:

Suppose a mixture of 500 cc. of *A*, boiling point 60°, with 500 cc. of *B*, boiling point 100°, is distilled into four receivers, each receiver taking in its turn 250 cc. of distillate. It is assumed for simplicity that there is no loss of material during the entire process, and that no azeotropic mixture is possible.

FIRST DISTILLATION

	Fraction 1	*Fraction 2*	*Fraction 3*	*Fraction 4*
Boiling range	70–75°	75–82°	82–89°	89–94°
Yield	250 cc.	250 cc.	250 cc.	250 cc.

Since the boiling ranges of these fractions depend upon the amount of condensate that flows back from the upper walls of the boiler, the above figures might vary in different trials. The schedule is merely a reasonable illustrative assumption.

Fraction 1 is now returned to the boiler and redistilled. About 200 cc. of this passes over at a lower and narrower range of temperature, arbitrarily "cut" at 65° to 68°. When the 68° mark is reached,

distillation is interrupted.   Fraction 2 is now placed in the boiler along with the residue of Fraction 1.   Distillation is resumed, and about 75 cc. of distillate collected over the same range, 65° to 68°. Fraction 3 is now added, and from this only 25 cc. is obtained, 65° to 68°.   Finally Fraction 4 enters, and this yields only 10 cc., 65° to 68°.   Total 310 cc. for the new first fraction.

The residual boiler contents are now distilled into three additional fractions to be labeled Fractions 2, 3, 4 below.   It is noted that the first and last of the four fractions are large and that each has a relatively narrow range of boiling temperature.

SECOND DISTILLATION

	Fraction 1	*Fraction 2*	*Fraction 3*	*Fraction 4*
Boiling range	65–68°	68–81°	81–94°	94–97°
Yield	310 cc.	180 cc.	190 cc.	320 cc.

The process just described for the second distillation is now repeated three times with results as follows:

THIRD DISTILLATION

	Fraction 1	*Fraction 2*	*Fraction 3*	*Fraction 4*
Boiling range	62–64°	64–81°	81–96°	96–98°
Yield	370 cc.	125 cc.	130 cc.	375 cc.

FOURTH DISTILLATION

	Fraction 1	*Fraction 2*	*Fraction 3*	*Fraction 4*
Boiling range	60–62°	62–81°	81–98°	98–99°
Yield	425 cc.	70 cc.	75 cc.	430 cc.

FIFTH DISTILLATION

	Fraction 1	*Fraction 2*	*Fraction 3*	*Fraction 4*
Boiling range	60–61°	61–80°	80–99°	99–100°
Yield	480 cc.	20 cc.	20 cc.	480 cc.

Fractions 1 and 4 in the fifth run are nearly pure A and B, respectively.   Fractions 2 and 3, being of mixed composition, may be discarded unless there is a new run in prospect, in which case they would merely be added to the new raw material.

It is seldom that a scheme such as that outlined above is used without the aid of a fractionating column.   The addition of the

column would simply mean that the results above shown would be obtained in fewer distillations. The principle of repeated distillation is valuable, however, even though it may be applied only to a partial extent in actual laboratory practice. There are also other schemes of dividing, pouring back, etc.; see Robinson's **Fractional Distillation.**

74. Distillation through a Fractionating Column. Suppose that the flask shown in Fig. 1 contains a mixture of benzene (b. pt. 80.6°) and toluene (b. pt. 111°), two similar hydrocarbons. Figure 2 shows the boiling point-composition data for this system, in close agreement with Raoult's law. The letters in Fig. 1 refer to the same mixtures and temperatures as the respective letters in Fig. 2.

Let A represent the original mixture of benzene and toluene, which is boiled, producing vapor of composition A' which in turn escapes from the boiler. Striking the walls of the relatively cool column, A' starts to recondense. Such initial recondensation would mean the appearance of a small amount of whatever liquid mixture is normally at equilibrium with A'. But we already know that A and A' are at equilibrium, and therefore the first condensate will be A, as marked near the bottom of the column. The newly formed A runs back into the boiler.

In order to extract a supply of A from a vapor of A' composition, however, it is plainly necessary to strip the vapor A' of a relatively large part of its toluene content. The residual vapor, not yet condensed, must therefore be richer in benzene, although reduced in
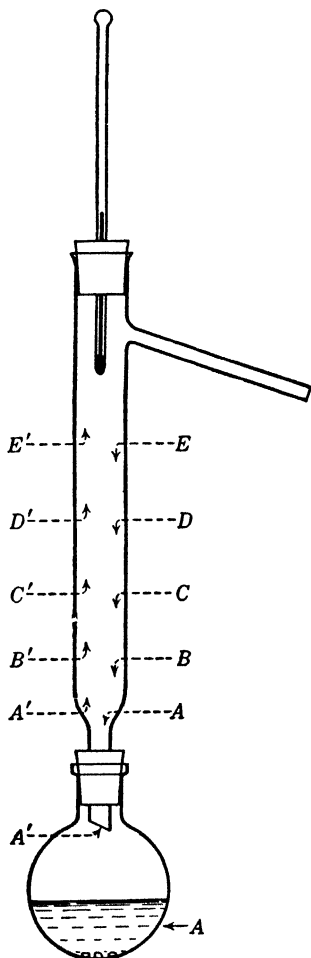
Fig. 1. Fractionation

quantity; it is also cooler than A'. Let its composition be shown as B', nearer to the benzene axis of Fig. 2 and lower on the temperature scale. But B' is merely another of the various vapor mixtures which may be at equilibrium with certain liquid mixtures, as plotted in Fig. 2.
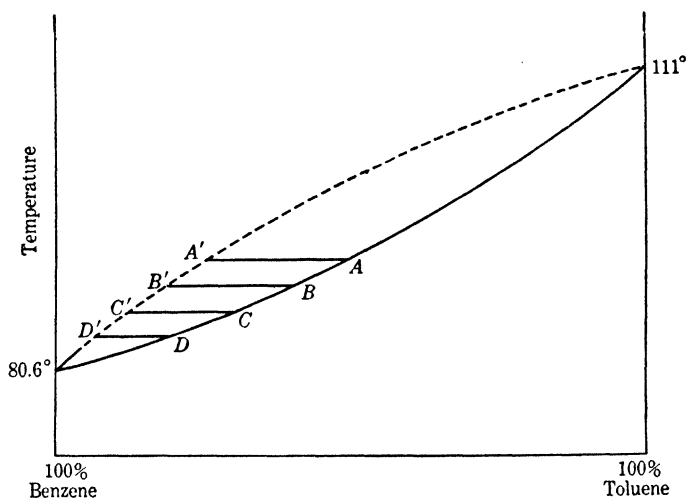
Fig. 2. Boiling Point—Composition Diagram

Vapor B' rises to a higher level in the column, and again partial recondensation occurs. Another quantity of condensate, relatively rich in toluene, runs back into the boiler. The residual vapor is altered in composition to the state C'; then to D', E', etc. Finally at the top of the column almost pure benzene emerges into the side stem and passes to the condenser. At the same time the temperature has been falling continuously until it has reached almost 80.6°.

Unfortunately so little vapor actually reaches the top that the process is very inefficient. Nearly all goes back as condensate to the boiler. A more rapid and more distinct separation is desired. The column is now packed with beads, and the distillation repeated with a new supply of the original benzene-toluene mixture.

75. Effect of Adding Beads. The ascending vapor of composition A' as usual suffers partial recondensation at the bottom of the

column. It thus produces some liquid A and itself becomes B'. Again the surviving vapor B' rises, this time for a short distance through the glass beads, and produces as usual some liquid B. So far the process resembles that in the simple column.

Liquid B, however, does not drop into the boiler immediately. It is detained by the beads for a short time but soon reaches the lowest level of the column, where the atmosphere about the beads
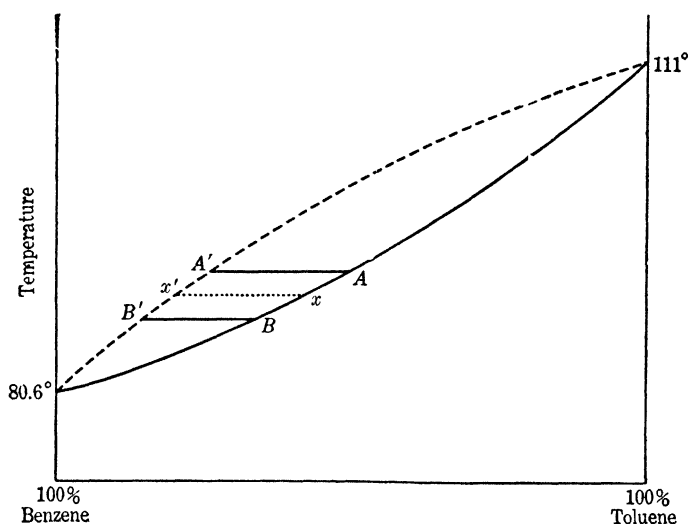
Fig. 3. Distillation with a Column Containing Beads

consists of vapor A'. Figure 2, however, shows that liquid B is not at equilibrium with A'; nor is it at the same temperature as A'.

Whenever a liquid and a vapor, each made up of the same components, but not at equilibrium with each other, are nevertheless allowed to meet, there will be a transfer of material from one phase to the other in the attempt to reach equilibrium. In the case at hand B contains too much benzene to be at equilibrium with A'. It will give up part of its benzene to the rising vapor A'. Similarly A', too rich in toluene to be at equilibrium with B, will give up toluene to liquid phase B. Figure 3 now shows the change.

Since the liquid recently designated as B is now richer in toluene (and somewhat warmer as well), it has the new composition X. A',

stripped of a certain amount of toluene (and somewhat cooler), changes to X'. But X and X' are on the same horizontal level, and thus they are at equilibrium. The process of interchange is at an end. Liquid X simply drips from the beads and falls into the boiler.

The important fact in the above scheme of operations is that A' has been transformed into a vapor richer in benzene with little or no loss in volume and without the necessity of additional length of column. The credit goes to the beads for their service in detaining the falling liquid B, breaking up its mass, and allowing time for interchange of components so that the vapor can be enriched in benzene.

If A' can be converted into X' at the lowest level of the column, there is no good reason why the next higher zone of beads cannot convert X' into B'.

Returning to Fig. 1 and 2, one sees the possibility of continuing the process through C', D', and E', and at last producing nearly pure benzene, which emerges into the side stem and passes to the condenser.

76. Temperature Change. Changes in **temperature** have much to do with the behavior of the system, as well as changes in composition. Accordingly, the operation of the column may be re-described from the viewpoint of temperature:

As before, vapor A' rises into the column, is cooled, and yields a partial condensate of A. The residual vapor B' again rises, yielding another partial condensate B. The relatively cool B slowly falls into the hotter zone of A' vapor. The temperature in this zone is above the boiling point of the falling liquid B. Naturally, therefore, B will boil, just as it would boil if placed in the midst of heated air from a burner. As it boils, B of course gives up vapor rich in benzene, and itself becomes rich in toluene.

The "boiling" of B caused by the heat transferred from A' is only half the story, thermally speaking. Since B is cooler than A' it serves as a sort of condenser upon which hot A' may deposit some of its less volatile substance. If now the evaporation of B just matches in quantity the condensation of other material upon B, no significant change in volume of either B or A' will occur—but a great change in composition.

77. Holdup of Liquid. Although the beads perform valuable service in separation of components, they introduce a serious diffi-

culty by holding up an appreciable mass of condensate. The boiler goes dry prematurely, and there is no further opportunity to fractionate the mass of condensate still held between the beads. Industrially such holdup is of little importance, since plenty of material lies in reserve. There is thus no objection to a very long column, running to the height of a four-story building or standing out in the
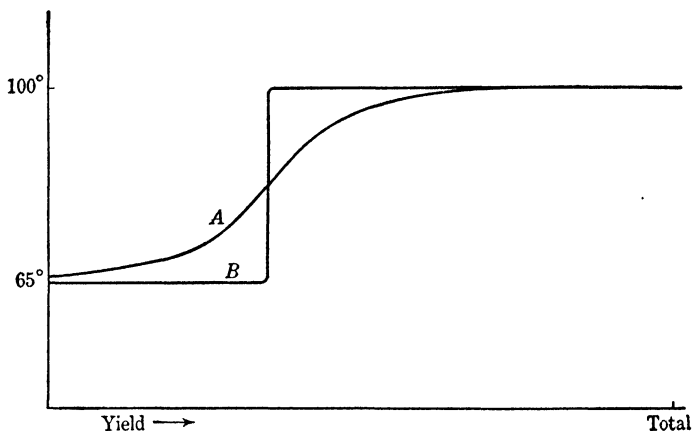
Fig. 4. Distillation of a Mixture of Methyl Alcohol and Water

weather like a cylindrical tower. Sharp fractional "cuts" are thus practical. In the laboratory one must resort to special designs to get comparable results.

To avoid holdup in the laboratory the Vigreux design (Fig. 5 § 39) is popular. In other models the general idea of a spiral passageway through the column seems to be of considerable value.

78. Distillation Curves. The comparative efficiency of distillation with and without a column is illustrated by curves showing the boiling points (as measured at the top of the column) at different times during a distillation. In the adjoining figure, boiling temperature is plotted vertically, and the yield (at each temperature measurement) horizontally. The liquid distilled was a mixture of 36% methyl alcohol and 64% water. Curve *A* is that obtained when the mixture is distilled from a simple flask. Curve *B* is that obtained by slow distillation with a special fractionating column. (See *Ind. Eng. Chem.* **20,** 420 (1928).)

Curve B indicates that the temperature of distillation remains almost constant at 65°, the boiling point of methyl alcohol, until nearly 35% of the original solution has been distilled. While the next few drops of distillate are being collected, the temperature rises rapidly to 100°, indicating that little remains in the boiler except water. Finally the second horizontal portion of the curve shows that practically pure water is being collected.

In practice the sudden change from such a temperature as 65° to a much higher value like 100° may not proceed smoothly unless heat is at once applied more intensely. A low adjustment of the burner, adequate for the low-temperature part of the process, may not suffice to distil water. Thus the sudden exhaustion of the volatile substance may cause a suspension of distillation. Cool air surges back from the condenser, causing the thermometer to behave erratically and indicate temperature values which have no significance in the experiment.

An example of such comparison in distillation is given in the acetone experiment (§ 241).

When two liquids show a slight positive deviation from Raoult's law, not sufficient to cause an azeotropic minimum boiling point, as illustrated in the methyl alcohol and acetone examples mentioned above, it is comparatively easy to perform a distillation of the B type pictured in Fig. 4. Contrariwise, irregular cases where the vapor and liquid curves lie closer together present difficult problems in fractional distillation. For example, it is easier to separate acetone sharply from water than acetic acid from acetamide (§ 269), despite the fact that the boiling-point difference in the second case is more than double that of the first.

79. Insulation. One of the most serious problems in the operation of laboratory columns is that of excessive cooling. In cases where a common Hempel column, 30 or 40 cm. long, does not give the desired fractionation, one naturally proposes a long column— perhaps 1 or 2 meters in length—or as long as the ceiling height in the laboratory permits. Unfortunately it is difficult to get an ordinary vapor through so long a column. The whole mass is recondensed. To remedy this situation one may insulate the outer surface of the column with magnesia-asbestos "lagging" in the manner commonly practiced with steam pipes, or adopt the more elegant method of surrounding with a vacuum jacket.

80. Azeotropic Mixtures with Fractionating Column. If the constant-boiling mixture of two components is distilled through a column, no change in composition occurs. The fact that a column has been interposed in the line has no bearing upon the situation.
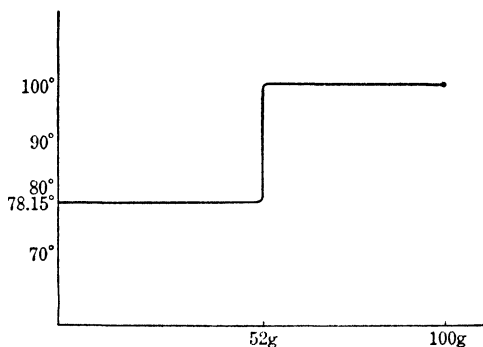
Fig. 5.   Distillation of 100 g. of a 50% Solution of Ethyl Alcohol Through an Efficient Column

The results obtained are the same as those from a simple distilling flask.

On the other hand, if the mixture of these particular components does not have the azeotropic composition, fractionation will occur. For example, if aqueous ethyl alcohol (50%) should be distilled through an ideal, highly efficient column, 96% alcohol would be steadily received in the condenser until the boiler was completely stripped of alcohol. The boiling temperature would then rise to 100°, and water would then pass over until all the remaining liquid had been distilled, as shown in Fig. 5.

81. Negative Deviation. If a mixture shows negative deviation from Raoult's law, but is not of azeotropic composition, there will also be fractionation. This time the *first* distillate will be of one pure component. For example (Fig. 6):

As already noted in § 68, chloroform (b. pt. 61.2°) and acetone (b. pt. 56.6°) form a constant-boiling mixture (b. pt. 64.7°, ratio 80 to 20 g.). Suppose a mixture of 40 g. of chloroform and 40 g. of acetone is distilled through an ideal column. At first pure acetone passes over until just 30 g. has left the boiler. The balance is of the azeotropic composition, 10 g. of acetone + 40 g. of chloroform.
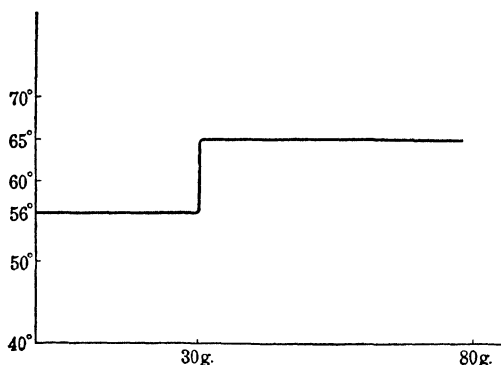
Fig. 6. Distillation of Acetone-Chloroform Mixture through a Column

Fractionation ceases, and the entire residue will distil uniformly at 64.7° to the end.

82. Fractionation under High Pressure. Recently it has become of industrial interest to distil fractionally mixtures of substances having very low boiling points. For example, the separation of propane (b. pt. − 45°) from its natural mixture with isobutane (b. pt. − 11°) and n-butane (b. pt. + 1°) is desirable in the manufacture of liquefied fuel gas for domestic use in the country. Such an operation might be conducted at high expense with the aid of liquid air or solid carbon dioxide. If, on the other hand, the mixture of hydrocarbons is confined in high-pressure steel apparatus, the range of boiling temperature may be elevated to common temperatures. Obviously the boiling kettle, fractionating column, condenser, and receiver must all be under pressure. The product is pumped into steel tanks for retail sale.

STEAM DISTILLATION

83. The distillation of two nonmiscible liquids in one vessel affords an excellent method of vaporizing a relatively involatile substance at a low temperature. Usually one of the liquids is water; therefore the practical problem is to cause a relatively high-boiling organic liquid to pass over with steam at a temperature near 100°. The organic substance in question may be unstable at its own nor-

mal, but high, boiling point. The possibility of its distillation with steam in the vicinity of 100° is thus attractive.

Before considering the customary process of using an external steam service, it is perhaps better to describe the behavior of two nonmiscible liquids when boiled together in one flask. Although one
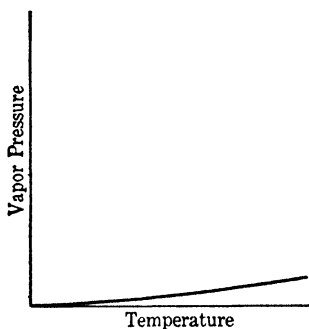
Fig. 1. Vapor Pressures of
       Iodobenzene
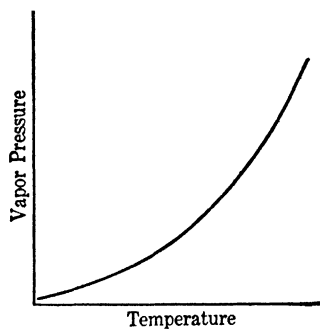
Fig. 2. Vapor Pressures of
       Water

of the liquids is usually water, such a limitation is not at all necessary in the following discussion.

The very fact that neither of the two liquids dissolves appreciably in the other is evidence at once that they do not obey Raoult's law. The situation may almost be regarded as an extreme case of "positive deviation" in which the combined vapor pressures are abnormally high. An example is seen in the distillation of a mixture of iodobenzene and water, two mutually insoluble liquids whose vapor pressures are represented in Figs. 1 and 2.

Iodobenzene and water behave independently of each other, although in the same vessel. Each exerts its own full vapor pressure in addition to that of the other component. Necessarily the combined vapor pressures of the two will reach 760 mm. before the temperature reaches 100°. To find the boiling point of the mixture, invert Fig. 1 and place it directly below Fig. 2, using the same horizontal or temperature axis, as in Fig. 3.

The line DE is graphically equal to 760 mm. pressure. For the sake of simplicity, move DE along to the left and downward until it just fits between the curves for iodobenzene and water, as at AC.

The intersection X marks the point where the sum of the vapor pressure of water (AX, 714 mm.) and that of iodobenzene (XC, 46 mm.) is 760 mm. This condition happens to occur at a temperature of 98.25°. The boiling point of this two-phase system is thus 98.25°.
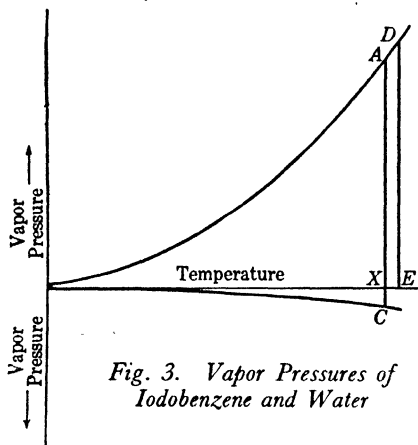
Fig. 3.   *Vapor Pressures of Iodobenzene and Water*

It does not matter how much of each liquid is present in the mixture. The above figures apply as long as both kinds of material are present.

If the iodobenzene is now replaced with a relatively nonvolatile substance like bromonaphthalene, the boiling point of the mixture will be nearer to 100°. The higher the normal boiling point of the organic component, the more closely the temperature of steam distillation approaches 100°. A low-boiling liquid, on the contrary, will boil together with water at a lower temperature. For example, a mixture of toluene (b. pt. 111°) and water boils at 85°. In general the boiling point of a mixture of nonmiscible liquids is below the normal boiling point of the more volatile component.

The variation of boiling point noted in cases of this type causes difficulty in the identification of certain organic substances when they are first distilled from crude reaction mixtures. For example, when n-butyl bromide is distilled from a mixture of sulfuric acid, butyl alcohol, water, and organic salts, as described in § 222, the boiling point of the mixture proves to be low. It gives no definite clue to the composition of the distillate prior to the purification of the desired product.

84. Efficiency of Two-Phase ("Steam") Distillation. The lines AX and XC in Fig. 3 measure the relative yields of water and iodobenzene, respectively, as collected in the receiver. In this case there will be 46 moles of iodobenzene obtained for every 714 moles of water. The truth of this simple deduction hinges upon Avogadro's law. Barring slight deviations from the simple gas laws, each mole-

cule, regardless of size or kind, exerts the same individual vapor pressure—or partial vapor pressure—after escaping from the boiler. The partial vapor pressures of 46 and 714 mm. thus simply measure respectively the relative numbers of each species of molecule passing to the condenser.

The ratio of 46 to 714 cited above at first seems unfavorable in the attempt to obtain a large yield of iodobenzene in a short time. When one notes, however, that 46 moles of iodobenzene weigh 9.38 kg., whereas 714 moles of water weigh only 12.85 kg., the contrast is seen to be not great. The distillation is efficient, as over 42% of the distillate will be of the desired iodobenzene.

In practice it is not customary to boil a mixture of water and the desired substance. As indicated in the practical directions for conducting the process (§ 43), steam is usually generated in a separate vessel. No change in principle is involved, however. The passage of a current of steam into an organic liquid at once introduces liquid water. The turbulent mixture of water, organic compound, and mixed vapors may be regarded as the practical equivalent of the contents of a simple flask where two liquids are being boiled together.

Actually the practice of using an outside source of steam is preferable. Direct heating of a glass vessel containing the two liquids might cause decomposition of the organic component. It might cause bumping. When the process is being used to purify a tarry preparation, direct heating might cause fracture of the flask at a point where the tar would stick and become scorched.

85. Distillation with Superheated Steam. Occasionally a liquid has so slight a vapor pressure at 100° that no adequate quantity can be obtained without the distillation of an unreasonably large volume of water as by-product. In such a case distillation with superheated steam may be employed.

Steam is passed through hot tubes and raised in temperature to 125°, 150°, or such higher temperature as may be necessary. It is then passed through a refractory liquid and carries large quantities of the desired vapors into the condenser. The yield does not depend on ratio of vapor pressures in the systematic manner described in § 83. The hotter the steam, the more of the refractory liquid will be swept out in the form of vapor.

As a practical conclusion, it may be stated that compounds which are insoluble in water, do not react with water, and exert an appreci-

able vapor pressure may be distilled in a current of steam, yielding a two-phase distillate from which water may be removed mechanically.

Problems on Fractional Distillation

1. Suppose you distilled a mixture of 50 g. of formic acid and 50 g. of water through an ideal fractionating column at a constant rate. Sketch approximately the curve you would expect to obtain, plotting time elapsed against boiling points.

2. Answer a question like Prob. 1 in which carbon tetrachloride and methyl alcohol are substituted for the formic acid and water.

3. One sample of a pentane-hexane-heptane mixture (light petroleum distillate) was exposed to the air until half of the material had evaporated. Another sample of the same mixture was distilled in the ordinary manner, without fractional reflux, until half of the material had passed into the condenser. Do you think that the contents of the distilling flask at this point would have the same composition as the residue from simple evaporation? Why?

4. In cases where a fractionating column is being used, why is the separation of two liquid components more readily effected by *slow* distillation than by a more rapid operation?

5. What does the position of the side stem on a distilling flask have to do with the efficiency of fractional distillation from such a vessel?

6. Assuming that only a mediocre fractionating column were available, which working pressure would permit the sharpest separation of bromobenzene from p-dibromobenzene in an equimolal mixture—760 mm., or reduced pressure in the region of 30 to 50 mm.? Why?

7. Draw a possible boiling point-composition curve for a mixture of two components whose slight positive deviation from Raoult's law does not cause an azeotropic solution to be possible, but makes separation by fractional distillation easier to perform than in the case of pentane-heptane.

8. Assuming that a highly efficient column were available, sketch a design for distillation apparatus which would continuously deliver pure benzene and pure toluene to storage vessels, given an indefinite supply, 24 hours a day, of a mixture of the two as raw material.

9. Explain why a large reflux ratio is favorable for efficient fractionation with a column.

10. Make a reasonable approximate estimate of the boiling point of each of the following mixtures. Figures chosen should be consistent with each other as well as with general principles:

(*a*) One mole of *n*-propyl bromide and one of water.

(*b*) One mole of *n*-propyl bromide and three of water.

(*c*) One mole of α-bromonaphthalene and one of water.

(*d*) One mole of bromobenzene and one of water.

(*e*) One mole of ethyl bromide and one of *n*-propyl bromide.

11. Suppose a mixture of 10 moles of *p*-dibromobenzene and 90 moles of water were distilled until one mole of the former had passed into the receiver. How much water would simultaneously be distilled?

12. A quantity of *n*-heptane contained 0.5% of suspended water. What fraction of the hydrocarbon must be distilled before the residue becomes dry?

13. Draw vapor-pressure curves to show how the yield of α-bromonaphthalene, from steam distillation, could be improved, in relation to water simultaneously distilled, by use of superheated steam.

CHAPTER 8

Washing and Extraction of Organic Preparations

86. The operations of washing and extraction are alike in principle, but slightly different in purpose. A mass of material, either solid or liquid, is mixed with a solvent which thereupon withdraws from that mass one or more constituents whose removal is desired. If the material so withdrawn is an undesired impurity, the process is called "washing." If it is valuable, and thus being preserved, the process is usually termed "extraction."

WASHING

87. A solid is washed usually as it lies upon a filter, the wash liquid being allowed to fall upon the finely divided mass and pass through. A liquid preparation is usually shaken with the wash liquid in a separatory funnel. The wash liquid is necessarily not miscible with the liquid preparation. Usually it is water or some more or less aqueous electrolyte, while the preparation is of the "oil" type, only very slightly soluble in water. In this normal case the procedure is as follows:

A separatory funnel of ample capacity is mounted in a ring on a common stand. The barrel and plug of the stopcock are dried with cloth and lightly treated with a firm, viscous stopcock lubricant which is not rapidly dissolved by common organic solvents. The liquid preparation and the wash solvent are then shaken together thoroughly in the funnel, after which the two layers or liquid phases are allowed to separate. If the wash solvent is denser than the organic liquid it may conveniently be run out through the stopcock, and the process can be repeated as often as desired.

If the organic liquid is more dense, as in the case of ethyl iodide which has just been washed with dilute aqueous sodium hydroxide, the denser liquid is run out into a flask for temporary storage, and

the wash liquid is *decanted from the top of the funnel. In no case does proper technique permit both liquids to pass through the stopcock and funnel stem.* If the washing is to be repeated, the once-washed liquid is returned to the funnel.

EXTRACTION

88. In extraction the desired organic compound is usually but not necessarily in an aqueous solution, in which case the extracting liquid is of the "oil" type. **Warning.** If the extracting liquid is volatile, a hazard immediately appears when the two liquids are mixed in the funnel, particularly if the material is warm. The shaking operation causes a sudden development of excess pressure inside the funnel. The glass stopper may be lifted and a spray of liquid blown into the face of the operator.

For example, should diethyl ether be quickly poured into a funnel containing both an aqueous solution and considerable air, a two-liquid-phase system would be immediately set up. Following the approximation that ether and water are mutually insoluble, the principle used in steam distillation (§ 83) would hold; that is, the vapor pressure of ether would suddenly be *added* to the pressure of air plus water vapor, which naturally was 760 mm. at the outset. But the vapor pressure of ether at ordinary laboratory temperatures runs from 400 to 500 mm. This calls for an excess pressure in the funnel of sufficient magnitude to cause trouble.

The experienced operator shakes the stoppered funnel gently at first, so that the excess vapor pressure will be developed slowly. He then inverts the funnel so that the pressure may be relieved by opening the stopcock for a moment. The stopcock is again closed, and the shaking of the funnel again followed by relief of pressure. After the atmosphere in the funnel is saturated with the solvent vapor, further shaking, either with or without addition of new solvent, develops little or no added pressure. Finally the well-stoppered funnel is vigorously shaken to permit the maximum possible transfer of the desired substance to the extracting solvent.

It is not always easy to separate the two layers at this point, owing to colloidal interference. It may be necessary to strain the total liquid mass through cheesecloth, glass wool, or other coarse medium, or to add salt to break an emulsion.

When the two layers have separated distinctly, the next operation depends on relative densities, just as noted in the case of washing:

(*a*) *Extracting Solvent of Lower Density.*   Run the denser aqueous liquid into temporary storage and *decant* the extracting solvent from the top of the funnel.

(*b*) *Extracting Solvent of Higher Density.*   Run off the solvent as soon as the extraction has been performed, leaving the aqueous solution in the funnel.

Diethyl ether has been the principal solvent employed for extraction in organic laboratories for many years.   As suggested in § 142, it has special value because it is able to dissolve a small amount of water.   The main virtue of ether, however, lies in its low boiling point (35°).   It is very easily expelled from an ethereal extract.

In elementary practice the extreme volatility and inflammability of diethyl ether lead to wasteful evaporation and fire hazard.   In recent years di-isopropyl ether has been offered commercially.   Its higher boiling point (67.5°) signifies a much lower fire hazard, and this solvent is recommended for use of beginners, particularly in crowded laboratories.

89. Explosion Hazard from Ether Peroxide.   When an ether is allowed to stand for some time in contact with air, a small fraction of the solvent combines with oxygen to form a dangerously explosive ether peroxide.   The danger from this unstable compound is greatest just at the conclusion of a distillation of impure ether, when the relatively nonvolatile peroxide becomes concentrated in the distilling flask.   Not only ethyl ether, but other ethers form peroxides. Isopropyl ether is perhaps even more hazardous than ethyl ether. It should be observed, however, that ethereal distillations of the types described in the aniline and phenol experiments, where one does not evaporate ether alone to dryness, do not seem to make trouble.   The large liquid residue at the moment of final riddance of ether seems to eliminate the danger.

The presence of peroxide in ether is detected by shaking a sample of the solvent with an equal volume of 2% potassium iodide and a few drops of dilute hydrochloric acid.   Iodine is liberated.   The undesirable compound is eliminated by distilling the ether in steam from a flask containing sodium hydroxide solution.   Beware of ether which has been standing for several months in a partly filled

bottle, exposed to light and air. (See *J. Chem. Education*, **13**, 494 (1936).)

90. Recovery of Extracted Material. First of all, the extract is dried (see § 112) before elimination of the extracting solvent. Should the extract be very dilute and of considerable volume, a problem arises as to size of vessel for the process of evaporating the solvent. So large a flask is required to hold the extract that the final small residue of the liquid organic preparation cannot be distilled economically. Serious loss as residual vapor will occur.

To obviate this situation, a small distillation outfit of the type shown in Fig. 4, § 33, is adopted. A distilling flask is chosen, of the size appropriate to the expected volume of the liquid organic preparation. The extract, which is of much greater volume, is run gradually into the flask as the solvent passes over in distillation. A water bath may be required if the solvent is inflammable. Finally the desired liquid product, free from solvent, is distilled in the standard manner after a thermometer has been substituted for the dropping funnel.

91. Theory of Extraction. Since the organic compound desired in an extraction is appreciably soluble in both water and the extracting solvent, a problem arises. Given a certain reasonable allowance of solvent, should this quantity be used in one operation or be divided into portions for repeated extraction? The extraction of phenol from aqueous solution by ether serves as an illustration.

Phenol is distributed between the two solvents, water and ether, as soon as the extracting solvent and aqueous solution are shaken together. The ratio of the concentration of phenol in ether to that in water is known as the "distribution coefficient," or "distribution ratio." For simplicity in an illustrative calculation, it is assumed that the coefficient of phenol is 3 in ether and water. (Note that the two solvents involved must be mentioned in proper order whenever a figure for distribution coefficient is reported.) That is, the concentration of phenol in an ether layer is about three times that in the adjacent water layer. In dilute solutions this is approximately the same as saying that phenol is three times as soluble in ether as in water, comparing ratios of solute to solvent. This assumption facilitates calculation without serious error in general reasoning.

Given 40 g. of phenol dissolved in 1000 cc. of water. As a first experiment this is extracted with 1000 cc. of ether used in one portion. The two liquids are shaken together as usual.

Let x be the weight of phenol remaining behind in each cubic centimeter of the water. Then $3x$ will be the weight of phenol in each cubic centimeter of the ether. The total quantity of phenol is then readily set down:

$$1000 \times x = 1000x \text{ g. of phenol in water}$$
$$1000 \times 3x = 3000x \text{ g. of phenol in ether}$$
$$\text{Total} \quad \overline{4000x} \text{ g., which of course must equal 40,}$$
$$\text{the weight originally given}$$

Therefore
$$x = 40/4000 = 0.01 \text{ g.}$$
and
$$3000x = \textbf{30 g. of phenol extracted}$$

This is a 75% recovery in one operation.

Suppose the extraction experiment be repeated with a new supply of 40 g. of phenol in 1000 cc. of water. This time the 1-liter supply of ether is divided into two equal portions, with extraction in two operations:

First Extraction:

$$1000 \times x = 1000x \text{ g. of phenol in the water layer}$$
$$500 \times 3x = 1500x \text{ g. of phenol in the ether layer}$$
$$\text{Total} \quad \overline{2500x} \text{ g., which equals 40 g.}$$
$$x = 0.016, \text{ and}$$
$$1500x = \textbf{24 g. of phenol extracted}$$

This is a 60% recovery, 16 g. being left in the aqueous solution.

Second Extraction:

A similar equation will hold, but this time applying to the solution containing only the residual 16 grams of phenol:

$$2500x = 16 \text{ g.}$$
$$x = 0.0064 \text{ g.}$$
$$1500x = \textbf{9.6 g. of phenol extracted}$$

Addition of the two extract yields, 24 + 9.6, gives **33.6 g., a distinctly better total yield.**

In like manner one may easily prove that still better yields may be obtained by dividing the extracting solvent into three or more portions.

The following is a more formal treatment of the foregoing calculations:

Let x = weight of substance remaining in each cubic centimeter of the aqueous solution after one extraction.
K = distribution coefficient in solvent and water.
A = original weight of the substance sought.
V_1 = volume of extracting solvent.
V_2 = volume of aqueous solution.

Then KV_1x must equal the significant quantity desired in this calculation, namely, the total amount of substance obtained in one extraction, and V_2x = total wt. of substance left behind in the aqueous layer.

But

$$V_2x + KV_1x = A$$

from which

$$x = \frac{A}{V_2 + KV_1}$$

and

$$KV_1x = \frac{KV_1A}{V_2 + KV_1}$$

In the first calculation for phenol, single extraction,

$$KV_1x = \frac{3 \times 1000 \times 40}{1000 + (3 \times 1000)} = 30 \text{ g.}$$

In the second calculation, for two extractions,

(1) $$KV_1x = \frac{3 \times 500 \times 40}{1000 + 1500} = 24 \text{ g.}$$

(2) $$KV_1x = \frac{3 \times 500 \times 16}{1000 + 1500} = 9.6 \text{ g.}$$

In general, a very few extractions will suffice if the distribution coefficient is large. On the other hand, if the coefficient is much less than unity, many extractions will be required.

92. Extraction by Acid or Base. If it is desirable to extract an acid from a nonaqueous solvent, an aqueous alkali—usually sodium hydroxide—may be used. The acid is converted into the salt, which is almost certain to have a large distribution ratio in water and solvent. The acid may thus be extracted almost completely in one operation. Similarly a base can be withdrawn almost totally in one operation by extraction with an aqueous acid, such as dilute sulfuric acid.

93. Drying by Extraction. A peculiar application of the principle of extraction is found in the method of drying slightly polar liquids, such as diethyl ether to be used in Grignard syntheses. First the ether is washed to remove alcohol and other impurities, thus incidently becoming saturated with water. It would now require an excessive quantity of solid calcium chloride to serve as drying agent at this stage in the process, and ether would be lost in the mass of drying agent. On the other hand, an excess of saturated aqueous calcium chloride, shaken with the wet ether, will extract a definite fraction—much over 50%, but of course not all—of the water from the ether. In this manner most of the water is removed without mechanical trouble, and the drying may be finished with a small quantity of solid calcium chloride.

It should of course be noted that by such procedure ether cannot possibly be completely freed of water, even by numerous repeated extractions, since the extraction solvent (saturated calcium chloride solution) contains as a normal component the very substance one seeks to extract; that is, water. Equilibrium is established between the two phases. Thus the conventional algebraic calculations will not hold in the simple form already given.

Soxhlet Apparatus for Extraction

94. Devices obtainable on the market permit the simultaneous extraction of material and return of the recovered solvent to the extracting vessel. The liquid which has just been mixed with the material to be extracted is automatically carried to a vessel where the solvent is evaporated. The vapors of the solvent are condensed in the ordinary manner, and the distillate is allowed to return to the scene of the original extraction. The Soxhlet extractor is a good ex-

ample of such a device. It is possible to extract a mass of material with the equivalent of many liters of solvent, although the actual quantity of solvent in the apparatus may be limited to some small vaiue like 100 cc.

Questions

1. When 400 cc. of a dilute aqueous solution of allyl alcohol was shaken with 100 cc. of carbon tetrachloride, 2% of the alcohol was transferred into the tetrachloride layer. Calculate the (approximate) distribution coefficient of allyl alcohol in carbon tetrachloride and water.

2. The distribution coefficient of a certain organic acid in ether and water is 1. What weight of the acid could be extracted from a solution of 1 g. of this acid in 100 cc. of water if

(*a*) 60 cc. of ether were used in one portion?

(*b*) the same amount of ether were used in three 20-cc. portions?

3. Which would require the greater number of extractions from aqueous solution, hydroquinone or aniline? Why?

4. Salt is added to an aqueous solution of aniline to render extraction more efficient. Explain in terms of distribution coefficient.

5. An equimolal mixture of diethyl ether (see § 445) and *n*-pentane is poured into a separatory funnel partly filled with water. The funnel is now immediately stoppered and shaken thoroughly. Assuming that all material involved in the experiment was at 20° C., what would be the (approximate) pressure of the gaseous phase in the funnel? Why cannot this question be answered precisely?

6. Devise apparatus for continuous extraction of an aqueous solution by ether which would have the advantage seen in the Soxhlet device; that is, an arrangement whereby the equivalent of an indefinite volume of solvent is used, although actually only a limited supply exists.

CHAPTER 9

Isolation of Solid Products

95. A solid organic preparation usually first comes to attention as a precipitate, perhaps a mass of crystals, separating from a liquid reaction mixture. The resulting suspension is then filtered, preferably by suction. The Buechner funnel (*a*) is convenient for handling substantial quantities of a solid product, while the Hirsch funnel assembly (*b*) is suitable when both solid product and filtrate are of value and are to be preserved with minimum loss in transfer.

The circular piece of filter paper used in the Buechner funnel should be just large enough to cover the entire perforated plate without crumpling of the edges of the paper. Where crystals of appreciable size are to be collected, any common grade of porous filter paper is acceptable. Later, when suspensions of decolorizing carbon are to be filtered, paper of finer texture should be employed. Sometimes two sheets may be used together.

Buechner and Hirsch Filtration Apparatus

Suction is now applied with the aid of a connection of rubber tubing. This tubing must have a wall thickness sufficient to withstand complete evacuation without collapse. Without interruption of suction, a small amount of solvent is poured upon the paper. The appropriate solvent of course is like that from which the crystals are to be separated. Care is now taken that the paper clings tightly and uniformly to the plate, without chance for solids to slip under the paper and pass into the filtrate below.

The solvent, which promptly runs through the paper, is now re-

moved from the flask if its presence with the filtrate would be un-desirable.   Suction is resumed, and the reaction mixture is promptly poured upon the paper.   Ordinarily the mother liquor passes down rapidly, and if valuable it is set aside in a separate vessel before the crystals are washed.

Frequently one is unable to transfer the entire contents of the crystallizing vessel to the funnel in one operation.   Crystals adhere to the sides of the vessel.   It is now convenient to return part of the filtrate from the suction flask to the crystallizing vessel, and use it to flush the residual crystals into the funnel.   This operation may be re-peated as often as necessary.

After the filtrate has been set aside, the funnel, still holding the solid product, is replaced in the filter flask, ready for washing.   Nor-mally the wash liquid will consist of the same kind of solvent from which the solid product has just been isolated.   One should first moisten the crystal bed on the funnel with a limited portion of cold solvent without suction.   After a few moments in which the solvent thoroughly wets crystals and filter paper, suction is applied.   The wash liquid is quickly eliminated.

96. Change of Solvent.   After the crystal mass is washed on the Buechner filter it may still hold a substantial amount of residual solvent adhering to crystals, despite vigorous suction.   From 5 to 15% of the wet mass is likely to be liquid; much more in the case of finely divided or semicolloidal preparations.   If the solvent is non-volatile, it becomes desirable to wash with a volatile solvent so that the ultimate crystalline product may be thoroughly dried.   This new solvent must be miscible with the first.   For example, ethylene glycol might be washed out with methyl alcohol, but not with benzene. Care must be taken that this change of solvent is not made until the crystals have been washed once with a fresh supply of the original solvent.   (See § 95.)

In such cases it is desirable to press down the crystal mass.   This limits the amount of wash liquid required for the operation.   A glass stopper of "mushroom" type, held in inverted position, is a con-venient tool for this purpose.   There is usually a supply of such stop-pers in the storeroom, salvaged from broken bottles.

If the final crystalline mass is not easily shaken out of the funnel, it may be blown out if the advance precaution be taken to protect the mouth from direct contact with the funnel.   In such a procedure

the funnel is inverted closely over the dish which is to receive the crystalline product. The end of the stem is grasped tightly, and the mouth is pressed firmly against the top of the fist; or a short section of large rubber tubing is interposed between funnel and mouth.

97. Precautions. A safety bottle should be interposed between a filter pump and filter flask; otherwise a backwash of water from the pump into the filtrate may occur. Such misfortune may easily take place when the pump is drawing vigorously from a flask under a clogged filter. A sudden fall in water pressure, caused by the wide opening of a near-by faucet, diverts the water of the filter pump into the highly evacuated filter system. Furthermore, should the operator fail to disconnect the pressure hose before turning off the filter-pump valve, he will certainly cause the undesired backwash.

If the flask is connected to a piped vacuum system, great care must be taken to avoid overfilling the flask with mother liquor. Carelessness of this sort results in the passage of filtrate into the vacuum line, with possible injury to vacuum equipment.

98. Use of a Fluted Filter. Occasionally a solid product is so finely divided that it tends to work its way through the pores of the filter when suction is applied. In other cases colloidal, viscous material is present, and the attempt to filter forcibly drives the viscous material down upon the filter in an impervious, varnishlike layer, blocking further passage of filtrate. One may then resort to the fluted filter. This device is prepared from loosely fabricated filter paper in the manner shown by the accompanying diagram. Despite the absence of a suction pump, natural drainage through a porous fluted filter may in the end afford the more rapid filtration. The fluted filter is mainly used, however, in handling a hot saturated solution where the evaporation and cooling caused by vacuum filtration would cause sudden, premature precipitation of the crystalline product.

99. Preparation of a Fluted Filter. Select a circular piece of filter paper of two to two and one-half times the diameter of the conical funnel to be used. In folding this paper in fluted form, be very careful that the hands are dry, lest a weak point develop at the bottom of the finished cone. It is well not to fold the paper too sharply near this point—but very sharply in the wider folds above.

When the folding is finished and the filter opened out, its pointed

bottom should be very carefully moistened just before the filter is placed in the funnel. The whole paper cone may then be pushed down gently into the funnel so that there will be a slight constriction of folded paper at the place where the hazard of breakage is greatest. If the liquid undergoing filtration is strongly acidic or alkaline this precaution is particularly valuable. Care should be taken not to
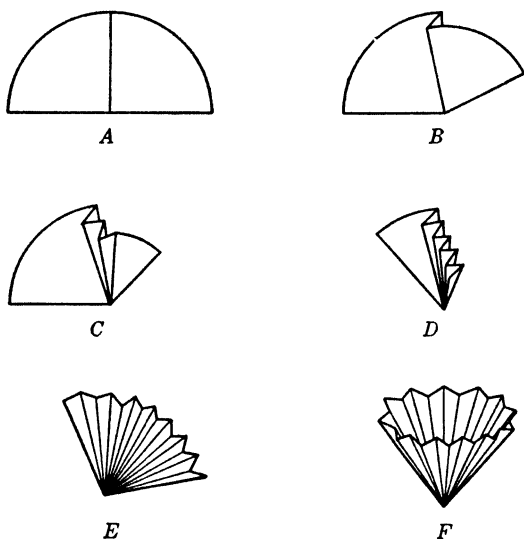
Folding of a Filter

overdo this constriction, lest the passageway be choked and the value of fluting be lost.

In cases where recrystallization occurs so rapidly that the funnel stem may become choked with solid product, the stemless funnel is popular. Actually the long stems of standard commercial funnels are a requirement of analytical chemists, while organic chemists usually find stemless funnels more convenient.

100. Vessels for Recrystallization. The solid preparation is now dissolved in a heated solvent. The resulting solution is then cooled, whereupon the solid reappears, usually in crystalline form. This operation requires a covered vessel. Both flasks and beakers are widely used for the purpose. The modern Pyrex conical flask, which

stands much more thermal abuse than old-time European ware, is perhaps the best vessel for the purpose now available. The straight sloping wall of the conical flask permits easy access with a tool sometimes needed for dislodging crystals, while the small mouth minimizes escape of volatile solvents. A "crystallizing dish," or open
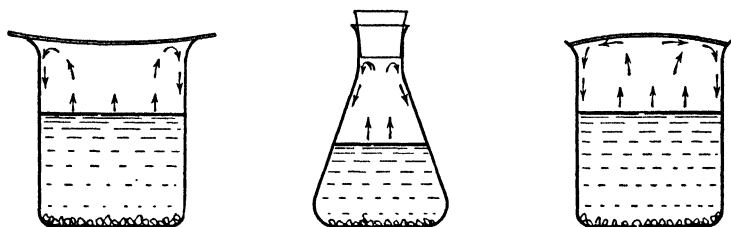
Recrystallization in Covered Vessels

beaker, is particularly undesirable. In such a vessel the solvent evaporates excessively at the margin of the solution, and impure crusts of solid matter accumulate.

With the conical flask, crystals are likely to form first on the bottom where the initial cooling is most rapid. Furthermore, vapors of solvent will be automatically distilled for some time from the hot surface of the liquid to the upper walls of the vessel which are cooled by the atmosphere and thus act as a condenser. The freshly condensed solvent washes down the walls and may even cause a layer of very dilute solution to form at the top. Under such conditions crystals will be less likely to grow at the top where they are least desired. If a beaker is used instead of a conical flask, a watch glass is used as a cover.

101. Hazards in Recrystallization. Warning. The recrystallization of material from inflammable solvents in unprotected vessels is not permissible. The flask for recrystallization should be connected to a reflux condenser, with precautions against fire much like those suggested in §§ 34 *ff*. Not only does the reflux condenser reduce the fire hazard, but it also permits a prolonged attempt to dissolve a solid in a limited portion of solvent without waste by evaporation. Recrystallizations from alcohol, benzene, acetone, etc., should all proceed under reflux, with water bath or steam cone for heating

medium, while operations with diethyl ether or carbon disulfide call for special precautions.   (See § 34.)

102. Procedure in Recrystallization.   If preliminary solubility tests have been made in test tubes, the proper quantities of solid and solvent may simply be placed together in the vessel, mixed thoroughly, and heated to the boiling point.   In the absence of solubility data, a small part of the solid may be placed with the estimated requirement of solvent.   When the mixture reaches the boiling point, successive additional portions of solid and solvent are added until the whole quantity has been dissolved in the minimum quantity of solvent.   If the substance has the habit of crystallizing rapidly, it may be advisable to add solvent slightly in excess of the above requirement.   This will allow time to filter before crystals could appear in an inconvenient place.

Some compounds crystallize so rapidly that there is not time for the hot solution to pass through a filter.   In such cases a steam- or hot-water-jacketed funnel is prescribed to prevent crystallization in the wrong place.

The boiling saturated solution may contain insoluble impurities, thus requiring filtration.   If the solution does not deposit crystals rapidly upon cooling, it may be filtered at this point in the Buechner funnel.   Otherwise a sudden deposition of crystals may choke not only the funnel stem but, worse yet, the small holes in the Buechner filter plate.   The fluted filter, or for smaller amounts a paper folded in the ordinary fashion, is then more serviceable.   If this process does not yield a clear liquid, decolorization with carbon (§ 109) may be needed.

If the flask containing the filtrate from the above-described procedures is now stoppered as shown in the illustration, and allowed to stand, the desired crystalline preparation should accumulate.   If large crystals are desired, the crystals and liquid should be heated to the boiling temperature until all crystals are redissolved.   The heating is then discontinued, and the flask is wrapped with a towel to prevent rapid cooling.   If finer crystals are desired, the hot saturated solution is stirred vigorously and cooled rapidly—perhaps with the aid of cold water or an ice bath.

103. Slow Crystal Formation.   Occasionally a solution will not deposit crystals on cooling, despite the fact that it is already highly

supersaturated.   The presence of a protective colloid, perhaps a viscous substance, causes this trouble in many cases.   If a so-called "seed crystal" of the desired substance be introduced, crystallization sometimes starts and continues until equilibrium is reached.   Seeding is illustrated in the recrystallization of benzil (§ 340).   In troublesome cases the seeding process may be combined to good advantage with refrigeration in an ice-salt bath at $-10°$ to $-15°$.   Cases have been known where a supersaturated solution, contaminated with "tar" which was acting as a protective colloid, required hours of refrigeration with ice and salt for the first crystallization.   When the crystalline product was subjected to recrystallization, the time of crystallization was shortened to a few minutes.

Crystallization is often started by scratching the inner wall of the crystallizing vessel with a glass rod.   The operation seems to line up the sluggish molecules in their normal geometrical pattern, and crystals form on the scratch lines.

104. Theory of Recrystallization.   Ordinarily the molecules of impurities in a solid preparation will not fit into the geometrical design of the crystals of the principal substance itself.   Furthermore, the solution is not likely to be saturated with respect to any one impurity.   Accordingly, upon recrystallization the newly formed crystals emerge to the actual mechanical exclusion of the impure residual solution (the so-called "mother liquor").   Naturally the new crystals are comparatively pure, provided they are not allowed to grow so large and complex that they **occlude,** or box in, drops of mother liquor.

If the hot solution is cooled rapidly, a multitude of fine crystals is likely to appear.   Within limits this is a desirable outcome, as no single crystal is large enough to occlude impurities.   On the other hand, it is possible to go too far.   If the desired substance is very insoluble in the cold solvent, its particles may be so numerous that they become colloidal.   The colloidal particles not only tend to obstruct a filter, but also **adsorb** undue amounts of impurities on account of the excessive surface area exposed by the finely divided solid.

. Sometimes a slow growth of large crystals affords the only practical method of separating two compounds that are very much alike in solubility.

105. Choice of Solvent. Almost always the solubility of a prepa-
ration increases with rise in temperature. The accompanying figures
illustrate common cases. Solubility is plotted against temperature.
As with vapor pressure, the solubility rises at an accelerated rate.
Occasionally the slope of the curve is gentle, as in Fig. 2. This means
that the solvent is less adapted to the process of recrystallization than
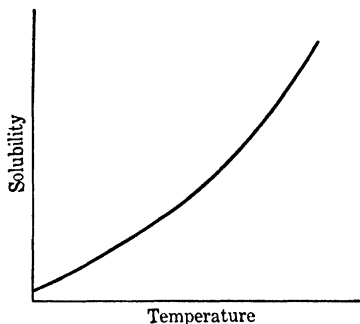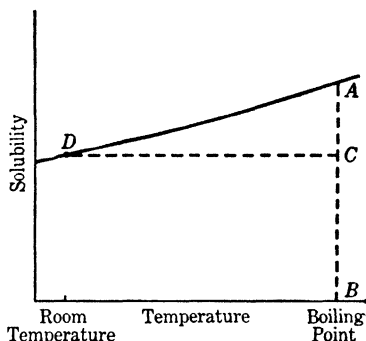
Fig. 1   Fig. 2

Solubility-Temperature Diagrams

the one represented in Fig. 1. The loss upon recrystallization in the
second case is readily computed:

Suppose the solid in question were heated with just enough of the
solvent (water) to dissolve the material at the boiling point. The
saturated, hot solution is now cooled to 20°. The content of the
solution of the substance at 100° (boiling point) is represented by the
line *AB*, or 30 g. At 20° the content is represented by *BC*, which
indicates 20 g. per 100 g. of solvent. Accordingly two-thirds of the
original substance remains in solution, while but one-third, repre-
sented by *AC*, or 10 g., is obtained as crystalline material.

On the other hand, the solubility of a substance may be 30, or
even 50, times as much at the boiling point of the solvent as it is at
20°. Recrystallization may then be accomplished with a yield above
95%.

The selection of a solvent of the type shown in Fig. 1 usually
means the choice of one not too closely resembling the substance to
be recrystallized. Nonpolar substances are often better recrystal-

lized from ethyl alcohol than from ether or ligroin, for example. On the other hand, if the solvent and solute are too much unlike, as with water and *p*-dibromobenzene, it is impossible to dissolve enough under any circumstances for effective work.

106. Nonvolatile Solvent. If a crystalline product has been deposited from a nonvolatile solvent, it becomes desirable to wash with a volatile solvent, as suggested in § 96, but with special attention to technique. For example:

A crude product is recrystallized from nitrobenzene, b. pt. 210°, low-boiling solvents having proved unsatisfactory. The residual mother liquor clinging to the new recrystallized product contains impurities. If the crystals were washed first with the volatile solvent benzene, there would be danger of precipitation of certain impurities which, though soluble in nitrobenzene, do not dissolve appreciably in benzene. The crystals are therefore washed first with nitrobenzene, to remove the impure mother liquor, and then with benzene to remove the nitrobenzene. The benzene, being volatile, disappears promptly upon drying.

LIST OF COMMON SOLVENTS

Solvent	Boiling Point	Solvent	Boiling Point
Diethyl ether	35°	Benzene	80°
Carbon disulfide	46°	Isopropyl alcohol	82°
Acetone	56°	Petroleum solvents	30° to 175°
Chloroform	61°	(variable)	
Methyl alcohol	65°	Water	100°
Di-isopropyl ether	68°	Toluene	111°
Carbon tetrachloride	76°	*n*-Butyl alcohol	118°
Ethyl acetate	77°	Glacial acetic acid	118°
Ethyl alcohol	78°	*m*-Xylene	139°

107. Separation of an "Oil" from Solution. If a substance has a low melting point, the laboratory worker may have trouble with the separation of a second liquid phase, commonly called an oil, instead of the expected crystalline mass. Students very commonly get the impression that some strange foreign substance has put in an appearance or that the preparation has decomposed. Actually there may be nothing but the known solute and solvent present. A clear understanding of this phenomenon depends upon a study of melting

and solidification (Chap. 12).   Accordingly the explanation is postponed, to be taken up as a special topic in Chap. 13.

108. Use of Mixed Solvents.   Sometimes an organic compound dissolves either too freely or too sparingly in any one available solvent.   Mixtures of solvents may then be serviceable.   The following solvent pairs are often used:

Alcohol—water.

Benzene—ligroin.

Acetic acid—water.

Ether—alcohol.

Ether—petroleum ether.

The solid is usually first dissolved in the solvent in which it is more soluble.   The second solvent of the solvent pair, in which the solid is less soluble, is now added slowly until crystallization is imminent.   During all this procedure the temperature is maintained at a relatively high value, perhaps near the boiling point.   Cooling now causes a substantial separation of the desired solid.

Inexperienced workers, anxious for a large yield of recrystallized material, often overdo the performance just described.   For example, a compound is dissolved in quantity in hot alcohol, and water is added to unwarranted excess.   Practically the whole of the original preparation, impurities included, is thrown out precipitately as an amorphous mass.

A hydrocarbon solvent, such as benzene or light ligroin, might be paired with ethyl alcohol provided the latter is absolute or nearly absolute.   If the alcohol contains a substantial—and uncertain—quantity of water, such a mixed-solvent plan should be avoided, since the resulting solution is likely to separate into two liquid phases, making trouble in the ultimate process of crystallization.

CLARIFICATION OF SOLUTIONS

109. Laboratory Procedure.   If the solution of an organic preparation is discolored or turbid, it may often be clarified with the aid of decolorizing carbon.   This process usually is most effective when the solvent is water, least with ligroin and petroleum ether.

The solution is boiled with a small quantity of the powdered carbon, perhaps a few grams per liter of solution.   Care is taken not to add carbon to a superheated solution, or the latter may suddenly

foam excessively and boil over. After 5 to 10 minutes boiling the mixture is filtered through a fluted filter, as described in § 99. As the process of clarification normally accelerates the crystallization which is to follow, it may be necessary to consider such devices as the stemless funnel and the steam-jacketed funnel. In these devices premature crystals are less likely to form and be caught before the filtrate reaches the proper crystallizing vessel.

For aqueous solutions of considerable volume which do not deposit crystals rapidly on cooling, the Buechner funnel may be used. Great care must be taken to see that the paper is of close-grained texture and that the paper circle is wet with the proper solvent and neatly pressed down upon the perforated plate before filtration is started. Suction is then applied, and the suspension is carefully poured upon the center of the filter.

110. Function of the Carbon. Decolorizing carbon has at least two functions. First, it may hold viscous, tarry matter in a bulky porous form upon the filter. In this function the carbon has an important rival in diatomaceous earth, which is widely used for the purpose industrially. Diatomaceous earth probably deserves more attention in the laboratory than it usually receives.

The ability to adsorb finely dispersed particles from colloidal solutions is an equally important characteristic of decolorizing carbon. This property is of value not only in handling turbid solutions, but often in decolorizing certain transparent liquids which, although colored, look like true solutions. Actually these solutions contain undissolved matter, but in so fine a state of division that light is not greatly disturbed as it passes through the mass. Many of such colloidal solutions are brown in color.

Since brown is not a recognized primary color, it is suspected that no pure organic compound exhibits such a color. Even the brown dyes (cf. Bismarck Brown) are probably mixtures of substances. It is therefore the custom to regard brown tints as evidence of impurity which is very likely to adhere to crystals which may later be produced in the solution.

111. Commercial Carbon Preparations. Boneblack (animal charcoal) is the most widely known decolorizing carbon, but by no means the best. It has limited adsorptive power, and moreover gives trouble at times from lime salts which are normally present in

the commercial preparation. An acidic solution should never be treated with ordinary boneblack if the desired substance is to be obtained later by a process of neutralization. If such error were made, the calcium would first be extracted as the soluble acid phosphate, and pass into solution. Later tricalcium phosphate would be precipitated along with the organic preparation when the solution was neutralized. This situation is avoided by the use of boneblack which is washed in advance with hydrochloric acid. Much better than boneblack, however, are some of the modern carbon preparations such as "Norit," made from birch wood, "Darco," and "Nuchar."

At times an impurity may have so great a colloidal electric charge upon its particles that it is not readily adsorbed upon the surface of decolorizing carbon. A decided change in acidity of the solution may be of great benefit, suggesting that adsorbed hydrogen or hydroxyl ions were the cause of the difficulty.

If the appropriate reagent (alkali or acid, respectively) be added with the carbon, the offending adsorbed ion is removed, and the particles of impurity, thus discharged, go out with the carbon upon filtration. It is suspected that the efficacy of the alkaline purification of sulfanilic acid is explained in this way. (See § 302.)

Highly colored soluble substances, especially dyes of great molecular weight, frequently are colloidal in character, although they seem to form perfect solutions. Such colors may often be removed in limited quantity with the aid of decolorizing carbon.

Occasionally decolorizing carbon will adsorb an undue amount of the substance undergoing purification. This possibility will serve as a warning against excessive quantities where preparations of high molecular weight are involved.

CHAPTER 10

Drying of Organic Preparations

112. Liquids. The removal of free water, present either in solution or suspension in a liquid organic preparation, is called "drying." The preparation is placed in a conical flask of relatively large size, and particles of a suitable drying agent are well scattered over the bottom of the vessel. Every part of the shallow layer of liquid is thus near to some piece of the material. In chemical literature such a procedure is often called "drying over" the drying agent. After the preparation is dry, it is either decanted or filtered to eliminate the spent drying agent.

Hydrocarbons and other reduced compounds of the "oil" type dissolve water so sparingly that they are rapidly dried even by a mediocre drying agent, such as sodium sulfate. A compound like butyl alcohol, however, which dissolves a considerable amount of water, may not yield its water content even to an efficient drying agent until some hours have elapsed.

113. Drying by Distillation. Distillation of an organic preparation before drying is usually considered to be slovenly technique. Occasionally, however, drying is accomplished by the very process of distillation itself, where one needs to dry thoroughly only part of an ample supply of some high-boiling solvent. Often the liquid is of the oil type, and the water passes out rapidly by a process which might be called steam distillation in reverse. Aniline (b. pt. 184°) and nitrobenzene (b. pt. 210°) are rapidly cleared of water in this way, so that the major fraction of the distillate may then come over dry. Even benzene and toluene may be dried by distillation, though not so rapidly. Occasionally a small amount of a liquid preparation is dried by addition of a nonaqueous solvent like benzene, followed by distillation of the benzene, which carries out the water.

114. Solids. A freshly prepared wet solid is ordinarily dried in the open air. The crystals are spread on filter paper resting in an

open dish, and the whole is loosely covered for protection from dust. If the preparation will stand oven temperatures (as determined in advance with a small sample!) the process will be expedited. The laboratory steam bath is often useful—again after the precaution of a preliminary test. A simple modification of the steam bath, useful for small quantities of solid, consists of a relatively large watch glass resting upon a beaker of boiling water.

115. Drying under Reduced Pressure. Better than either of the above methods is that of drying in the vacuum desiccator. A

| Special Heavy Model | Scheibler Model | Pyrex Model; Heavy Wall |
| High Safety Factor | Low Safety Factor | High Safety Factor |
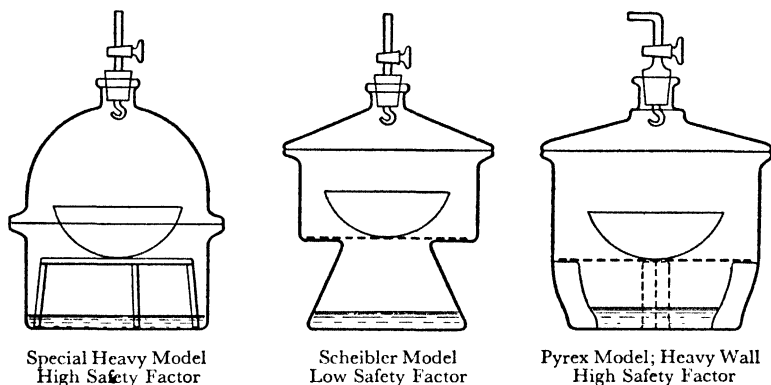
Vacuum Desiccators

suitable drying agent, usually concentrated sulfuric acid, is placed in the bottom of such a desiccator. A screen or perforated porcelain plate supports the dish in which the preparation is placed for drying. Air is pumped out until the residual pressure falls to 20 mm. or below. Under these conditions the molecules of water vapor travel through the space between the crystals and the sulfuric acid in much shorter time than is possible when a blanket of relatively dense air intervenes. Some desiccators are not well designed mechanically, and may not safely be exhausted to low pressures. Consult the instructor as to safety limits in evacuation; or see the commercial catalogue of the Fisher Scientific Company of Pittsburgh, Pa., which gives a critical appraisal of the hazards of different desiccators.

116. A Vacuum Oven is employed for drying a substance to the extreme degree required in precision analysis. One popular form of

this is known as the Abderhalden drying apparatus. In this arrangement a preparation is enclosed in a glass-stoppered, evacuated test tube surrounded by the hot vapors of a refluxing liquid. The water vapor coming from the crystals travels a short distance and meets a mass of calcium chloride or phosphorus pentoxide just outside of the heated zone.
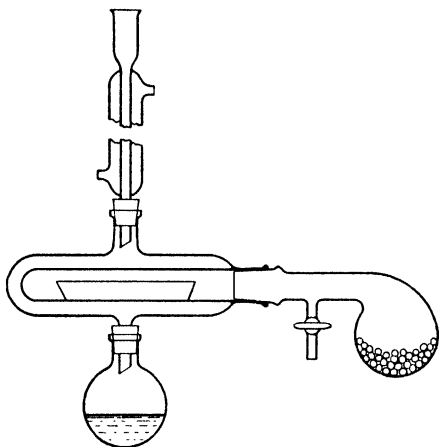
117. Theory of a Drying Agent. Drying agents may be divided, though not always with clear lines of distinction, into two types: (*a*) those which react in a fundamental manner with water to produce an entirely new water-free substance, usually by a nonreversible reaction; and (*b*) those which take in water of hydration reversibly.

Abderhalden Drying Apparatus

The drying of benzene with metallic sodium illustrates the first type of activity. The water is entirely broken up, and may not be recovered by an ordinary process. Calcium carbide is another reagent of similar type. When placed in aqueous alcohol or similar liquid, it converts the water into acetylene and calcium hydroxide. Phosphorus pentoxide, one of the most efficient, combines with water to yield one or another of the phosphoric acids. Calcium oxide, or quicklime, may be added to this class—or may be somewhat loosely treated as a substance of the (*b*) class which forms a hydrate reversibly.

118. Hydrate Formation. When one of the second class of drying agents comes into contact with water, it is said to bring into play its so-called "coordinate valences," by virtue of which it combines more or less firmly with the water. For example,
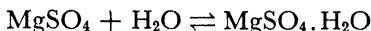
$$MgSO_4 + H_2O \rightleftharpoons MgSO_4.H_2O$$

The double arrow as usual indicates that the reaction is reversible, so that the conditions of equilibrium are of major consequence in this discussion.

If more water is added, the hydrate $MgSO_4 \cdot H_2O$ yields in turn the dihydrate, tetrahydrate, pentahydrate, hexahydrate, and finally as the upper limit the heptahydrate, or "Epsom Salt," $MgSO_4 \cdot 7H_2O$. Each of these compounds is a drying agent except the last one, which of course is already hydrated to the limit of its coordinate valences. Similarly other salts, such as calcium chloride and magnesium perchlorate, combine with water to form several hydrates. The number of molecules of water of hydration in other salts is not necessarily the same as in the cited example, however.

It is almost obvious that different salts have widely different efficiencies as drying agents. It is equally true that different lower hydrates of any one particular salt, such as magnesium sulfate, have widely variant values. From one theoretical standpoint the merit of a drying agent is shown by the **decomposition pressure** of the next hydrate above the substance in question. For example, the value of $MgSO_4 \cdot H_2O$ is measured by the decomposition pressure of $MgSO_4 \cdot 2H_2O$. The following table gives approximate values for the decomposition pressures of the hydrates of magnesium sulfate at 25° C.

$$MgSO_4 \cdot 7H_2O \rightarrow MgSO_4 \cdot 6H_2O + H_2O \quad 13 \text{ mm.}$$
$$MgSO_4 \cdot 6H_2O \rightarrow MgSO_4 \cdot 5H_2O + H_2O \quad 10 \text{ mm.}$$
$$MgSO_4 \cdot 5H_2O \rightarrow MgSO_4 \cdot 4H_2O + H_2O \quad 9 \text{ mm.}$$
$$MgSO_4 \cdot 4H_2O \rightarrow MgSO_4 \cdot 2H_2O + 2H_2O \quad 5 \text{ mm.}$$
$$MgSO_4 \cdot 2H_2O \rightarrow MgSO_4 \cdot H_2O + H_2O \quad 2 \text{ mm.}$$
$$MgSO_4 \cdot H_2O \rightarrow MgSO_4 + H_2O \quad 1 \text{ mm.}$$

The meaning of the above table is illustrated simply by the ideal experiment of introducing an excess of any of the above hydrates into an evacuated vessel. For example, if the dihydrate were so introduced, some of its molecules would break up according to the appropriate equation above, yielding the monohydrate, until the newly produced water vapor was sufficient in quantity to exert a vapor pressure of 2 mm. Or, approaching the problem from the opposite extreme: if the monohydrate were admitted to a vessel containing water vapor at 10 or 15 mm., a reverse reaction would start, and the dihydrate would be produced until the pressure had fallen to 2 mm. It is the latter type of experiment which is of major significance in the problem at hand, viz., the drying of organic preparations.

By analogy from the last experiment, the monohydrate of mag-

nesium sulfate will take water away from any surrounding fluid medium until the activity, or effective concentration of water, in that medium is cut down to a value equivalent to 2 mm. of ordinary water vapor.

Should an excess of the organic liquid (or other fluid medium) now be added, the monohydrate will continue to absorb water and maintain the 2 mm. maximum until it has all been converted into the dihydrate. Further addition of aqueous material at once offers opportunity for the formation of the next hydrate $MgSO_4 \cdot 4H_2O$. The vapor pressure limit is at once raised to 5 mm., however, and the drying from this point forward is not as thorough as before.

119. From this simple experiment two of the most important criteria of a good drying agent are at once revealed, as follows.

1. **Intensity** of drying.

2. Quantitative **capacity** for drying purposes.

Under caption (1) comes the major question—How low can the vapor pressure, and thus the water percentage, in a liquid preparation be taken by use of an ample supply of the given drying agent? Under (2) the question is—How much water can be absorbed by a given weight of the drying agent at a given intensity—that is, before it becomes necessary to go up to a still higher hydrate?

The answers to (1) come from the vapor-pressure tables; those to (2) simply require a little supplementary chemical arithmetic. In both cases wide differences exist between the values for different salts. Magnesium perchlorate trihydrate, for example, is a much better drying agent than magnesium sulfate dihydrate, despite its larger molal water content. The merit of the perchlorate lies in its great intensity, which is a specific property of the particular magnesium compound.

Unfortunately the organic laboratory worker has no simple way of knowing the aqueous activity, or escaping tendency, of water in his liquid preparations. He is thus unable to predict just the particular hydrate which will meet a given need. Furthermore, no certainty of hydrate composition exists in most common commercial preparations of drying agents, so that the exact behavior of a specific hydrate has little meaning in everyday laboratory practice.

120. Testing Drying Agents. A simple, practical method of appraising commercial drying agents is that of using them to dry sam-

ples of air. The air, previously moistened, is allowed to come into contact with the drying agent and is then analyzed for water content. The lower the final water content in the air sample, the better the drying agent from the intensity standpoint.

WT. OF H_2O LEFT IN ONE LITER OF GAS DRIED AT 25° C.

Phosphorus pentoxide, P_2O_5	less than 0.00002 mg.
Magnesium perchlorate, $Mg(ClO_4)_2$	" " 0.0005
Magnesium trihydrate, $Mg(ClO_4)_2 . 3H_2O$	" " 0.002
Potassium hydroxide, KOH fused	0.002
Aluminum oxide, Al_2O_3	0.003
Sulfuric acid, H_2SO_4	0.003
Magnesium oxide, MgO	0.008
Sodium hydroxide, NaOH fused	0.16
Calcium bromide, $CaBr_2$	0.2
Calcium oxide, CaO	0.2
Sulfuric acid, H_2SO_4 95%	0.3
Calcium chloride, $CaCl_2$ fused	0.36
Zinc chloride, $ZnCl_2$	0.8
Zinc bromide, $ZnBr_2$	1.1
Cupric sulfate, $CuSO_4$	1.4
Sodium sulfate, Na_2SO_4	12

Since 1 mg. of water contained in one liter of gas at 25° exerts approximately 1 mm. of partial vapor pressure, millimeter may be substituted for milligram in the foregoing table without error of significance in the phenomena under consideration.

COMMERCIAL DRYING AGENTS

121. Calcium Chloride. This well-known reagent is prepared industrially in "granular" form by strong heating, but without melting. It is porous, chalky, and serves not only by chemical reaction but as an absorbing agent. Where possible loss of liquid in a porous preparation is feared, "fused" calcium chloride is used.

This desiccant has a low enough vapor-pressure rating for ordinary drying of many liquids in organic chemistry, or for maintenance of a dry atmosphere in a desiccator used in quantitative analysis. On the other hand, calcium chloride is unsuited to the drying of alcohols, also some esters, which chemically combine with the salt. It is relatively unsuited for use in a desiccator whose

purpose is to dry a solid; for such purpose concentrated sulfuric acid is much more efficient.

Calcium chloride is somewhat slow in action, therefore not so suitable for drying a hydrocarbon as sodium sulfate, described below. This slowness of action is possibly due to the blanketing of each particle of the commercial product with a thin layer of solution formed out of the first small quantity of water received. If the wet pieces of calcium chloride are allowed to remain for a day or more in contact with the moist liquid, the moisture will strike into the mass, and a more permeable structure of solid will be produced—this time of a crystalline hydrate of low water content. The new hydrate itself is a good drying agent.

The industrial process of preparing anhydrous calcium chloride usually permits a slight amount of hydrolysis, yielding hydrogen chloride gas which escapes and causing the product thus to be contaminated with calcium hydroxide. This is of importance in organic combustion analysis, where such calcium chloride must be treated with carbon dioxide before use in determining water vapor.

122. Calcium Oxide. Quicklime is serviceable as a drying agent for the simpler alcohols, but by virtue of its high alkalinity is ruled out of most other possible applications.

123. Calcium Sulfate. Known commercially as "Drierite" (not to be confused with Dehydrite!), this compound was overlooked by chemists until recently. It is outstanding from the intensity standpoint, but unfortunately reacts at that intensity only to form the hydrate $2CaSO_4 . H_2O$, and thus combines with only 6.6% of its weight in water. It is excellent for difficult tasks like the final drying of oxidized compounds which were nearly dry to start with; *e.g.*, methyl acetate, formic acid, and acetic acid. The porous commercial product will absorb 10 to 12% of its weight in water in a common drying operation, where extreme desiccation is not essential. [See *Ind. Eng. Chem.* **25**, 1112 (1933).]

124. Magnesium Perchlorate. This costly but efficient drying agent is used principally to absorb water vapor in organic combustion analysis. It does not "channel" or run into irregular viscous masses in the manner of phosphorus pentoxide, its competitor in certain research fields where extreme desiccation is required. It is unsuitable as a general drying agent for organic compounds because

of the explosion hazard involved in mixing perchlorate with combustible matter. It is particularly dangerous to allow perchlorate to come into contact with acids, or aldehydes which may be converted into acids. Furthermore, magnesium perchlorate has too high a solubility in certain organic solvents. It is known commercially as "Anhydrone," and in the form of the trihydrate as "Dehydrite." [See *J. Am. Chem. Soc.*, **44,** 2255 (1922).]

125. Magnesium Sulfate. Neither investigators appraising drying agents nor the majority of supply dealers seem to have discovered this excellent reagent, which is probably the best neutral, low-priced desiccant available. Its complex series of hydrates (§ 118) indicate striking gradations in drying ability according to condition of material. Where calcium chloride is ruled out on account of formation of addition compounds, or where acidic and basic desiccants are not permissible because of catalytic difficulties, magnesium sulfate is a very useful resource; for example, with esters, nitriles, aldehydes, and ketones. The granular preparation is made by heating coarsely crystalline Epsom salt gently (150° to 175°) in an oven until it has lost a large part of its water of hydration; then to redness for complete desiccation. If one is not particular about preserving the neat granular form of the above product, he may save time by conducting a single rapid heating of Epsom salt in an evaporating dish, as described in § 182.

126. Phosphorus Pentoxide. This acid anhydride reduces water concentration so low that no remainder is assuredly detectable. Thus it serves as a standard of perfection in intensity of drying. It channels badly and is usually ruled out in organic synthesis because of its acidic character.

127. Potassium Carbonate. This moderately efficient drying agent is being superseded in many applications by magnesium sulfate, but is still useful with certain ketones, nitriles, etc.

128. Potassium and Sodium Hydroxides. For basic or inert liquids potassium hydroxide is an excellent desiccant. Sodium hydroxide is somewhat inferior to the potassium compound.

129. Sodium Sulfate. While at the bottom of the list in thoroughness of drying, sodium sulfate is neat in its action. Occurring in fine granules which are readily scattered through a mass of liquid,

it reaches emulsified water rapidly and thus quickly clears up suspensions of water in hydrocarbons, halides, etc. It is of little use in withdrawing water from oxygenated compounds, and entirely useless above 32.4°. (See § 18.)

130. Sulfuric Acid. This extremely effective reagent is rarely used for drying liquids but is widely employed for drying gases and for desiccator service. Great care must be taken not to allow organic material to be spilled from a container into the sulfuric acid of a desiccator. Within a few hours the sulfuric acid would react with the introduced material, generating sulfur dioxide and perhaps injuring the preparation being dried.

When used in a desiccator, sulfuric acid will absorb not only water, but alcohol. If alcohol is thus allowed to pass into the sulfuric acid, the acid should be changed before the desiccator is again used.

131. The **drying of the hydrochloride of a weak base** presents a special problem. Suppose such a preparation had just been separated from a strongly acid solution. The excess acid was necessary to prevent hydrolysis. The crystals are covered with residual mother liquor containing both water and hydrochloric acid. If they were placed in an ordinary sulfuric acid desiccator in the common way, so much hydrogen chloride gas would be liberated that there would soon be not even a partial vacuum. The drying process would be retarded. In such a case a dish containing a few pieces of solid sodium hydroxide is placed in the desiccator beside the vessel containing the preparation. The hydrogen chloride gas reacts with the sodium hydroxide to form harmless common salt, releasing water which is absorbed in the regular manner in the drying agent below.

132. Drying by Hydrolysis. Since the hydrolysis of a substance consumes water, it is sometimes possible to dry a liquid by conducting such hydrolysis therein. One of the best examples is seen in the process of converting ordinary "absolute" ethyl alcohol (99+ %) into extremely dry alcohol.

$$RCOOC_2H_5 + H_2O + NaOC_2H_5 \rightarrow RCOONa + 2C_2H_5OH$$

For this purpose ethyl formate is specially well adapted (see § 361), and diethyl succinate has also been used (E. L. Smith, 1927).

Questions

1. Metallic sodium reacts more rapidly with water than with ethyl alcohol. Why is it not considered a satisfactory reagent to convert aqueous alcohol into absolute alcohol?

2. Choose an appropriate drying agent for:

(*a*) Isopropyl alcohol.

(*b*) Benzaldehyde.

(*c*) An ethereal solution of *n*-amylamine. ·

(*d*) Chlorobenzene.

(*e*) Methyl cyanide.

(*f*) Ethyl formate.

(*g*) Toluene.

(*h*) Propionic acid.

3. Why is the extract of an organic compound dried before instead of after evaporation of the ether?

4. Why should a drying agent be removed from a liquid before distillation?

5. Under what circumstances might distillation be conducted without disadvantage with the drying agent still in the liquid?

6. Explain how carbon tetrachloride (b. pt. 76°) can be freed from water by distillation, in view of the fact that water boils 24° higher than the solvent in question.

7. In which liquid would the partial vapor pressure of water be greater, 99% aqueous amyl alcohol, or 99% aqueous ethyl alcohol? Give two reasons to support your conclusion.

8. What relation has your answer to Prob. 7 to the relative ease of drying the two alcohols?

CHAPTER 11

Solubility of Organic Compounds

133. Prediction of Solubility. Since it is impossible to find solubility tables for all the numerous combinations of solute and solvent, it is desirable to formulate rules to help estimate the solubility of any given organic compound in any given solvent.

In predicting solubility, most organic chemists use a sort of intuition based on the fundamental rule colloquially known as "like dissolves like." Stated more formally, this principle may be expressed as follows.

A substance is likely to be soluble in a solvent which it closely resembles in chemical constitution and physical characteristics. For example, hexane is very soluble in heptane; butyl alcohol in amyl alcohol; formic acid in acetic acid; propylene dibromide in ethylene dibromide. The likenesses here are obvious. On the other hand, butyl alcohol is very soluble in chloroform, whereas aniline hydrochloride is not. Questions naturally arise: Wherein lies the similarity of the alcohol and chloroform? And why are aniline hydrochloride and chloroform particularly unlike?

Several kinds of "likeness" influence solubility. If the solute resembles the solvent in most of these characteristics, it is likely to dissolve freely in that solvent. If unlike at many points, it will be relatively insoluble.

(a) *Degree of Oxidation by Oxygen.* The percentage of oxygen in a compound is perhaps the greatest single factor readily applicable in judging likeness of an organic solute and solvent. Substances containing little or no oxygen tend to be very soluble in solvents containing no oxygen. Substances of high oxygen content dissolve freely in solvents containing much oxygen. The unoxidized solutes, on the other hand, do not dissolve appreciably in solvents containing much oxygen, and vice versa.

For example, the molecules of hexene and glucose are both built

upon the same carbon skeleton, and thus at first glance seem to be alike. Each contains 6 carbon atoms and 12 hydrogen atoms.

Hexene $CH_3CH_2CH_2CH_2CH{=}CH_2$
Glucose $CH_2OH.CH.CHOH.CHOH.CHOH.CHOH$
$$O\mathbin{\vrule width 0pt}\text{———————————}\mathbin{}$$
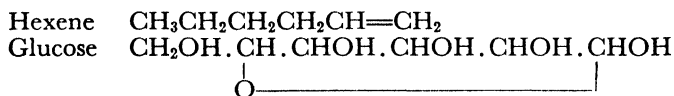
In contrast to hexene, glucose contains much oxygen. Accordingly, glucose is very soluble in water, but not in benzene or pentane. Hexene is very soluble, in fact miscible in all proportions with benzene and pentane, but almost insoluble in water.

(b) A substance of low **dielectric constant** is likely to be most soluble in a solvent of low dielectric, insoluble in one of high constant, and vice versa. For example, bromobenzene, dielectric constant 5.2, is miscible with carbon tetrachloride, d.c. 2.25; but it is almost insoluble in water, d.c. 81. This rule is little used, because of inadequate data. It is closely related to rule (c) given below.

(c) A polar substance is more soluble in polar solvents, less soluble in nonpolar solvents. Nonpolar solvents have corresponding solubility relations. The term "polar" describes a compound which behaves as though its molecule were charged electrostatically positive at one place, negative at an opposite location. Some of these are of the type called a "dipole," in which the center of positive charges in the molecule is not the same as that of the negative electrons, for example, methanol. Other polar compounds have such distinct positive and negative parts that the molecule actually dissociates into separate positive and negative fragments, which are of course the ions. Salts are thus the most strongly polar organic compounds.

Water, although slightly ionized, is highly polar. Accordingly various organic salts, such as aniline hydrochloride and sodium benzoate, are usually more soluble in water than their parent bases and acids, such as aniline and benzoic acid. These salts are usually insoluble in nonpolar solvents.

Aliphatic compounds with highly branched molecules tend to be somewhat more polar than straight-chain isomers. For example, 100 g. of water at 20° dissolves only 8 g. of n-butyl alcohol, 11 g. of isobutyl alcohol, but is miscible in all proportions with tert-butyl alcohol.

Two rules additional to those exemplifying the likeness principle are also important.

(*a*) A solute of low **molecular weight** is generally more soluble in a solvent than one of high molecular weight. Kerosene is less soluble than gasoline in ethyl alcohol, for example. Furthermore, since both solute and solvent may be liquids, this rule may be reversed—solvents of low molecular weight have relatively high dissolving efficiency.

(*b*) A solute of low **melting point** tends to be more soluble in solvents than one of high melting point. For example, phenol, melting point 43°, is far more soluble in water than is benzoic acid, a compound of somewhat similar structure and with more oxygen but which melts at 122°. Similarly, solids are ordinarily less soluble in a given solvent than liquids of similar chemical constitution. Even a given solid substance is less soluble in a solvent than the liquid form of that same substance.

134. Reaction Solvents. A substance tends to "dissolve" in a solvent with which it chemically combines. This is really another example of the likeness rule, but under a disguise. For example, benzaldehyde, C_6H_5CHO, a substance containing but little oxygen and having a fairly high molecular weight, is but slightly soluble in water, as one might expect (1 g. to 300 g. of water). It might be expected to be less soluble in aqueous sodium bisulfite solution, a highly polar medium. It reacts with the bisulfite, however, to form a new compound,

$$C_6H_5CHO + NaHSO_3 \rightarrow C_6H_5CHOH.SO_3Na$$
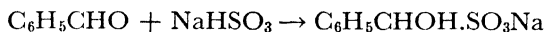
The new compound is obviously in part like sodium bisulfite in structure. Therefore it dissolves freely in the solution of that salt.

Similarly, β-naphthol ($C_{10}H_8O$), a substance with only a small percentage of oxygen, is but slightly soluble in water. It dissolves freely in aqueous sodium hydroxide, however, since the polar salt is formed.

Likewise, amylene is almost insoluble in water, but very soluble in fuming sulfuric acid, a highly polar liquid. It forms an alkylsulfuric acid compound, $C_5H_{11}HSO_4$.

The great solvent power of acetone is thought to be due in part to the ability of that compound to combine loosely with many solutes. No clear-cut, defined compound is produced, but the solute may be described as "solvated," just as many inorganic compounds are "hydrated" when crystallized from water. Acetone thus dissolves

resins, pitches, dried paint, varnish, lacquer, as well as a host of pure
organic compounds containing more or less oxygen.

135. Halogens. A chlorine atom, substituted for hydrogen in an
organic compound, usually gives a solubility effect much like adding
two or three carbon atoms to the original molecule. For example,
ethyl chloride in solubility relations is much like butane. With
bromine and iodine the weight effect is accentuated, though not in
any proportion subject to exact prediction. Ethyl bromide is much
like pentane, and ethyl iodide like hexane. These halides are there-
fore almost insoluble in water, but are miscible with ether, gasoline,
and such nonpolar solvents.

When three chlorine atoms are concentrated on one carbon atom,
as in chloroform, a very slight tendency toward the polar character
is observed. This solvent accordingly dissolves to some extent cer-
tain slightly polar compounds, such as alkaloids, waxes, etc.

136. Sulfur, Nitrogen. These elements give no striking solu-
bility effect of themselves unless they cause the formation of some
polar substance such as an acid, base, or salt. Ethyl mercaptan
(C_2H_5SH), for example, although a substance of low molecular
weight, is soluble only to the extent of 1.5 g. in 100 cc. of water.
Benzene sulfonic acid, on the other hand, is soluble in water, not be-
cause of the specific influence of the sulfur atoms, but because of the
oxygen content, the hydroxyl group, and the polar acid character.
Diethylamine, while devoid of oxygen, dissolves freely in water be-
cause it reacts with that solvent to form the diethylammonium ion
$(C_2H_5)_2NH_2^+$, a polar substance. (See Chap. 15.)

137. Double Bonds. Unsaturated hydrocarbons are very
slightly polar. They are thus slightly more soluble than paraffins
in water. Gasoline, for example, is miscible with 95% alcohol, an
aqueous solution, if the gasoline contains a high fraction of olefines
and aromatics. Paraffin gasoline, however, is not miscible with 95%
alcohol. This fact is of interest in certain foreign countries where
there is demand for such mixtures as motor fuel.

138. The Hydroxyl Group. Being a structural component of
water, the hydroxyl group has a profound influence favoring aqueous
solution. A great liking for water is seen in such hydroxyl derivatives
as glycol, glycerol, pyrogallol, glucose. Even a substance of such

great molecular weight as cane sugar (sucrose) is very soluble in water. Its molecule contains eight hydroxyl groups.

139. The Hydrogen Bond. If a hydroxyl group happens to be located in an organic molecule near a doubly bonded oxygen atom, the terminal hydrogen atom may be held loosely by that oxygen atom. This presumably forms an O—H—O bridge, which has decided influence on solubility. Such a hydrogen bridge structure does not favor aqueous solubility to nearly the extent exhibited by the simple hydroxyl group. For example, o-nitrophenol, whose molecular space model permits a hydrogen bond, has a solubility of only 0.3 g. per 100 g. of water, while its higher melting isomer p-nitrophenol dissolves to the extent of 1.6 g.

140. Solubility of Solids. Most of the foregoing rules apply much more consistently to liquid solutes than to crystalline substances. In the solid state the forces holding molecules together are so great, and yet so widely variant, that remarkable differences in solubility occur between very similar solutes. For example, the solubility of maleic acid at 25° is 78 g. in 100 g. of water. That of fumaric acid, its (trans-) geometric isomer, is only 0.7 g. The difference between the "cis" and "trans" structure seems to be related to the contrast in solubility.

141. Intermediate Solvents. Ethyl alcohol is the most important example of the intermediate type of solvent. Its value lies very largely in the fact that it frequently dissolves both polar and nonpolar substances, thus permitting their intermixture and possible speedy reaction. For example, benzyl cyanide is ordinarily prepared by the interaction of benzyl chloride, a nonpolar oil, with sodium cyanide, a polar, water-soluble salt. The addition of ethyl alcohol to the proposed mixture creates a liquid phase in which substantial amounts of both reactants may dissolve. The reaction is then completed in a comparatively short time.

142. Slightly Polar Solvents. Diethyl ether is a more useful solvent in the organic laboratory than pentane or hexane, although the latter two can be furnished in isomeric mixtures from oil refineries at much lower prices. Much of the superiority of ether lies in its oxygen content, which presumably enables the substance to dissolve a small amount of water (about 1 g. in 75 g. of ether). For example:

Suppose an amine, RNH_2, is to be precipitated from solution in the form of its hydrochloride salt (RNH_3Cl). Since the R group is of the hydrocarbon type, the amine is best dissolved in a nonpolar solvent. Hydrogen chloride gas is passed into the solution, and the polar salt is precipitated. If such an operation were conducted in pentane, or its equivalent petroleum ether, the newly formed salt would carry with it any water which might have entered during the admixture of reagents. The pentane would repel the water. If dry ether were used, on the contrary, a dry, crystalline salt would be obtained, and the small amount of water would stay in the solvent. A much neater preparation may thus be obtained.
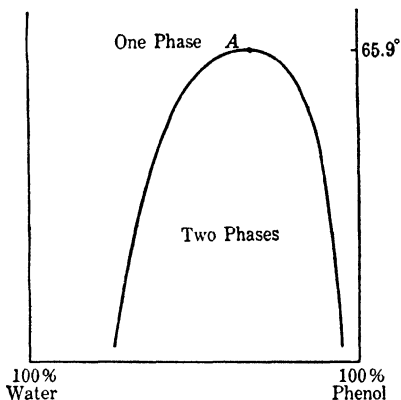
143. Solubility of Liquids in Liquids. If two liquid substances are similar and their mixture obeys Raoult's law, they will be miscible in all pro-

One Phase   *A*   65.9°

Two Phases

100%
Water

100%
Phenol

The System Phenol-Water

portions. Extremely unlike liquids, deviating positively to the highest degree from Raoult's law, are practically insoluble in one another. Other combinations of intermediate character, such as phenol and water or *n*-hexane and methyl alcohol, exist within certain limits of temperature as two-phase systems. One liquid layer is a saturated solution of the first substance in the second, while the other is a saturated solution of the second in the first.

The temperature limits above cited vary widely as the proportions of the two substances are varied. The accompanying illustration of the system phenol-water shows all possible temperatures and compositions which permit two phases to exist. Outside this (central) zone, phenol and water are miscible, that is, form one clear solution. The high point *A* (65.9°) is known as the critical solution temperature; that is, the highest temperature at which any mixture of pure phenol and pure water can exist in two phases.

144. Test for Water in Alcohol. In the experiment on absolute alcohol (§ 215), a special oil is mixed with alcohol in order to

locate the point A (as of the figure). The more water present, the larger is the two-phase zone. Point A rises regularly with each added percentage of water. The temperature value of each of the successive points A is then plotted against composition of the alcohol, resulting in the graph shown in § 215.

145. Questions. A series of questions is added to illustrate the application of the solubility rules. The first of these, questions 1 to 9, are straightforward queries dealing with cases in which the rules operate in agreement, or where but one rule has obvious significance. The second group, questions 10 to 20, refer to situations where the rules may seem to conflict. The answer to this type of question is likely to point out the fact that one rule, perhaps not the most obvious, is exerting such great influence that it completely reverses the prediction which some other rule invites.

Group 1

1. Why is acetone more soluble than diethyl ketone in water?

2. Why is n-butyl bromide less soluble in water than in n-propyl alcohol?

3. Why is iodobenzoic acid less soluble than benzoic acid in water?

4. Why is n-butyl alcohol more soluble than its isomer diethyl ether in water?

5. Why is phenol more soluble than dihydroxydiphenyl ($HOC_6H_4.$-C_6H_4OH) in ethyl alcohol?

6. If a 50% solution of n-propyl alcohol in water is saturated with potassium carbonate, it parts into two phases, each containing all three components. Explain on the basis of solubility rules.

7. How do we account for the fact that only the first three members of the series of normal primary aliphatic alcohols are miscible with water, whereas the first four normal aliphatic acids are miscible with the same solvent?

8. Why is excessive polymerization of synthetic resins embarrassing to the manufacturer trying to use these materials as ingredients of varnishes and lacquers?

9. Why is sec-amyl alcohol more soluble in water than n-amyl alcohol?

Group 2

10. Why is naphthalene more soluble in ethyl alcohol than in methyl alcohol, a solvent of less molecular weight?

11. Why is aniline, C_6H_7N, much less soluble than dipropylamine, $C_6H_{15}N$ in water?

12. Why is amyl alcohol less soluble in water than in concentrated sulfuric acid?

13. Why is methylamine hydrochloride, CH_6NCl, less soluble in propyl chloride, C_3H_7Cl, than in ethyl alcohol, C_2H_6O?

14. Why is starch, which contains at least half as many hydroxyl groups as carbon atoms, insoluble in alcohol?

15. Why is phenylene diamine more soluble than dinitrobenzene in water?

16. Why is water more soluble in propyl alcohol than in valeric acid, a more highly ionized solvent?

17. Why is it necessary to convert the metal lead into such an unusual and expensive compound as tetra-ethyl lead before applying it to the preparation of nondetonating ("Ethyl") gasoline?

18. Why is *p*-dibromobenzene less soluble in acetone than in diethyl ether, a solvent of greater molecular weight?

19. Why is ether more soluble in concentrated sulfuric acid than in water, a less ionized solvent?

20. Show how the very fact that *n*-butyl alcohol and water form a two-liquid-phase system proves that the mixture does not obey Raoult's law.

General Questions

21. Isobutene polymer and a concentrated solution of dextrine in glycerol have been recommended as stopcock lubricants. Which of these would be more desirable in a petroleum laboratory? Explain.

22. Why would a cotton garment be more safely cleaned by "spotting" with acetone than a rayon garment?

23. Suppose you dissolved a relatively small quantity of sodium palmitate (*n*-hexadecanoate) in an emulsion of kerosene and water. Predict the behavior of the palmitate ions; where would they be found after the mixture was shaken?

24. A mixture of 66 g. of phenol and 34 g. of water at 65.8° forms a rather stable emulsion, whereas the same mixture at 30° separates promptly into two layers. On a basis of density considerations, why is there such difference in behavior?

References

Oliver Kamm, *Qualitative Organic Analysis* (Wiley, New York, 1932), Chap. 2.

J. H. Hildebrand, *Solubility* (American Chem. Soc. Monograph), 1935.

CHAPTER 12

Melting and Freezing

146. The useful laboratory processes of (*a*) determination of melting point, and (*b*) crystallization depend in principle upon the phase changes of solid to liquid and the reverse. The first of these processes is usually conducted by heating a sample of the organic compound in question, together with a thermometer, in a heating bath. See § 203 for practical details of the procedure.

147. Liquid for the Heating Bath. In the hands of responsible workers, concentrated sulfuric acid is generally conceded to be the most economical bath liquid; but the personal hazard involved in handling hot sulfuric acid in glassware has led many laboratory supervisors to rule it out in favor of some less reactive liquid, such as glycerol or a nonvolatile oil. Olive and cottonseed oils have been used, but these liquids darken rapidly when used at high temperatures. Sulfuric acid may also darken on account of charring of organic matter accidentally dropped into the liquid. Such darkening, due to colloidal carbon or decomposed organic matter, is eliminated by adding a few centigrams (avoid excess!) of solid potassium or sodium nitrate, or even a drop of concentrated nitric acid, and heating until the contamination is cleared up by oxidation. Sulfuric acid yields offensive fumes at temperatures much above 150°.

Hydrogenation of vegetable oils increases their stability to some extent. As a result, such commercial products as "Crisco" are favored by some workers. Still better—if the melting points are all considerably above 60°—is hard-hydrogenated cottonseed oil. (See § 23.) A single portion of this oil may be used several times before it darkens too much to be useful. When it finally becomes too dark to permit ready observation of the melting-point tube, it may be set aside for service in common oil baths. For the latter application it is still as useful as ever.

More recently the heat-transfer liquid known as "Dowtherm"

(mixture of diphenyl and diphenyl oxide) has been highly recommended (Kamlet, 1942) for melting-point baths. Even this liquid will darken under strong heating, however.

148. Metal Block. The nuisance of a liquid heating bath may be eliminated by the use of a copper or aluminum block. The thermometer and melting-point tube are placed in holes drilled in the block. The high heat conductivity of these metals ensures prompt agreement in temperature of the crystals and thermometer. (See Morton, *Lab. Technique in Organic Chemistry*, p. 32.)

149. Theory of Melting-Point Determination. If an organic compound is pure and stable, the melting process all takes place at constant temperature, and the melting point is said to be "sharp." If the substance is impure, no single melting point is obtainable. The preparation gradually becomes liquid over a range of rising temperature, which usually lies below the known correct melting point of the pure substance. For example, pure naphthalene melts sharply at 80.09°; a sample containing a very small percentage of another substance, on the other hand, might begin to melt at 60° or 70° and become entirely liquid at 75° to 80°.

Not only is the melting-point determination a test of purity, but it is equally valuable as a means of telling which of the hundreds of thousands of organic compounds is the one being examined. If the melting point can be estimated within one degree, the determination eliminates over 99% of possible substances from further consideration. One leading company dealing in organic chemicals advertises in its catalogue the melting points and melting ranges of its merchandise and thus conveys much more useful information than by following the hackneyed custom of printing "C.P.," "Purified," or "Refined" after the listed items.

150. The Relation of Vapor Pressure to Melting Point. Both the liquid and solid forms of a substance exert vapor pressure, which rises with increase of temperature. The vapor pressure of a solid, however, rises faster than that of the corresponding liquid, as suggested in Figs. 1 and 2, showing the behavior of camphor.

For simplicity, suppose that a vessel is completely filled with a mixture of the above solid and liquid, maintained at constant temperature. Under such conditions molecules of the liquid, attempting to leave as though by distillation, can escape to no other place

than to the solid. The solid, attempting to evaporate, can go only into the liquid. If the first process were more rapid than the second, the material would all *solidify*. If the latter were more rapid, the solid would *melt*. To decide which phenomenon is likely to occur at any given temperature, superimpose Fig. 1 upon Fig. 2, obtaining Fig. 3. Since the two curves are necessarily not parallel, they must
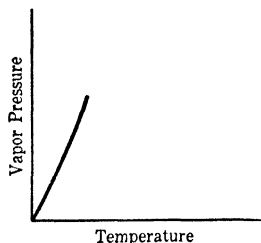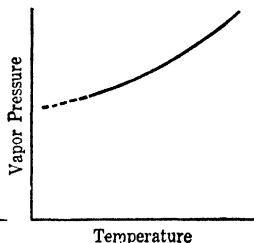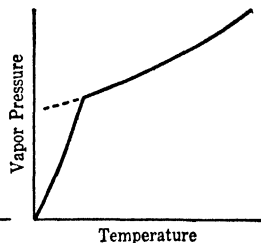
Vapor Pressures of the Solid and Liquid Forms of the Same Substance

intersect. This intersection is the melting point, which is an absolute constant if no extraneous pressure is involved.

The transformation of liquid to solid camphor will always be faster than that from solid to liquid provided the temperature lies below 179°. At temperatures above 179° the solid, having the greater vapor pressure, will be transformed more rapidly into the liquid phase. Only at the temperature of 179° are both vapor pressures alike, since two nonparallel curves of such simple character can intersect at only one point. Thus both rates of transfer are alike. Equilibrium is attained. Solid and liquid may remain together indefinitely as long as the system is neither heated nor cooled. The melting point is then defined as the temperature of this equilibrium.

151. Comparison of Practical Methods. The common "micro" method of determining melting point, while rapid and convenient, is not ideal from the standpoint of precision in locating the desired temperature value. If a considerable quantity of a substance is available, a more elegant and precise method may be employed. Twenty-five grams or more of the crystalline substance is partially melted, and the mixture of solid and liquid is stirred together in the form of a thin slush. If a thermometer is used as the stirring rod,

with complete immersion, the equilibrium temperature may be read off directly after a few minutes, provided there is an appreciable fraction of both phases continuously present. The whole outfit may be placed in a bath which is maintained at a fairly constant temperature not more than one or two degrees below the true melting point. Inside the inner vessel a constant temperature reading should be obtained in either case. The method is particularly good where the substance has a high heat of fusion, as do polar compounds.

No dotted extension of the vapor-pressure curve of a solid (Fig. 3) is shown. Such an extension would refer to a solid above its melting point. This condition does not exist, theoretically or practically. Superheating in the solid state is thus impossible.

152. Metastable Condition. The dotted curve (Fig. 3) represents the vapor pressures of a liquid below its freezing point. While theoretically impossible, this condition in practice may actually exist for an extended time. The liquid is then said to be "subcooled," or "undercooled" (sometimes "supercooled," a misnomer patterned after the term "superheated"). Subcooling sometimes deceives a beginner when he attempts to locate the melting point of a substance by cooling the liquid until it actually solidifies.

For example, pure acetic acid is supposed to solidify at 16.67°. When the substance is cooled, however, the temperature may reach 15° or even 10° before crystallization takes place. Finally the excessive cooling seems to force the crystallizing process, and the liquid suddenly and rapidly becomes solid. The temperature rises, but before it attains the correct equilibrium value the whole mass may become solid, and no significant thermometer reading can be made. The new solid will, however, melt promptly and sharply at 16.67°.

No dotted extension of the vapor-pressure curve of a solid (Fig. 3) is shown. Such an extension would refer to a solid above its melting point. This condition does not exist theoretically or practically. Superheating in this sense is impossible.

153. Behavior of Impure Preparations. Suppose a small amount of a second substance, naphthalene, is introduced into the equilibrium mixture of pure solid and liquid camphor—all at the temperature of 179°.

The naphthalene immediately dissolves in the liquid camphor, but not in the solid. Following Raoult's law, the vapor pressure of

the camphor is reduced. The activity or escaping tendency of camphor in the liquid state is reduced. Camphor will pass less readily from liquid to solid than from solid to the contaminated liquid. If the temperature were maintained at 179°, the net result would eventually be the complete melting of the solid camphor. But melting uses up heat; and as no heat is being added, the temperature falls.

The phenomenon may be represented as in Fig. 4, which is merely an extension of Fig. 3. The solid camphor at the outset
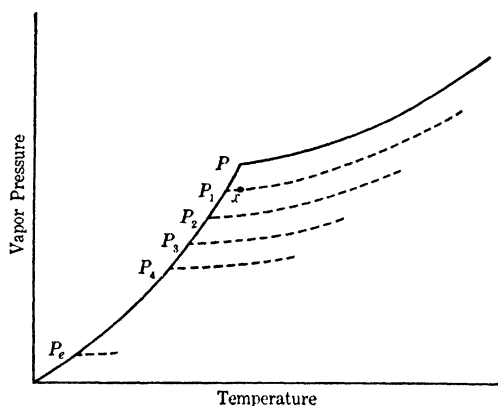
Fig. 4. Effect of Impurity upon Melting Point

had the vapor pressure and temperature (179°) marked as the point P. The impure liquid at this temperature would have the vapor pressure (that is, the partial vapor pressure of the camphor component only) marked as the depressed value x. Obviously a phase with pressure P cannot exist in the same vessel side by side with a phase of the same substance in which the pressure is lower than P, as at x. The solid represented at P would melt at once and go into the condition x.

But the melting of a solid requires heat. As none is supplied from the outside, the temperature of the mixture falls. The vapor pressure of the solid P, and of the impure liquid x, both fall at the rate marked by their respective curves until they meet at P_1. Here equilibrium ensues, and no further change is seen. Solid camphor

and the solution of naphthalene in camphor may remain together indefinitely at the temperature P_1 which is below the normal melting point of camphor.

Other points, still lower in temperature, such as P_2, P_3, and P_4, may be located, showing the equilibrium temperatures of solid camphor in contact with solutions of increasing naphthalene content.   Within reasonable limits Raoult's law now has a new application, namely, that the molecular percentage, and thus the molecular weight, of a compound may be measured by determining depression of melting point.

If the melting point of camphor can be depressed to P_1, P_2, P_3, P_4, a question naturally arises—How far may it fall? The limit is P_e, the eutectic point, which in this case is reached when the fraction of naphthalene reaches 42 mole per cent.   It is the temperature below which not even the impure liquid can persist; further refrigeration simply causes both components to so-

Fig. 5. *Melting Point—Composition Diagram*

lidify completely, and the experiment is done.   The eutectic point is better understood from a diagram plotted in a different manner.
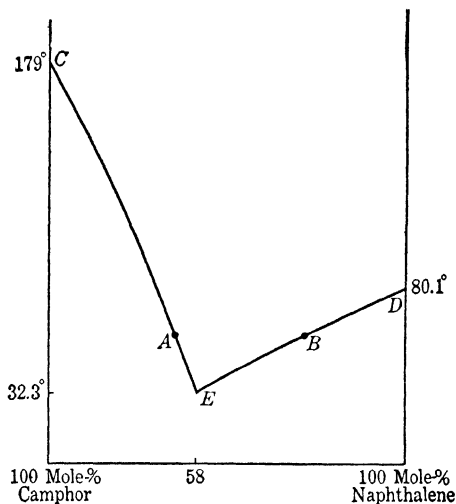
Melting point is plotted against composition throughout the whole range of possible mixtures of camphor and naphthalene. The curve CE indicates the successively lower melting points of camphor as naphthalene is added up to the maximum of 42 mole per cent impurity.   The curve ED shows the melting points of naphthalene with camphor considered as an impurity, up to 58 mole per cent.   Of course the 42% solution of naphthalene in camphor and the 58% solution of camphor in naphthalene are

identical. Therefore the curves must intersect as at E, the eutectic point, which happens to be 32.3°.

154. Melting Range. On the basis of the foregoing discussion it may now be easier to understand the successive phenomena in the conventional micro method of determining melting range of such a preparation as the impure camphor above cited. Figure 6 represents, ideally, a single crystal of camphor with a few small crystals of naphthalene (the "impurity") scattered over its surface. Nothing significant happens while the mixture is being heated up to the eutectic temperature. As soon as the eutectic temperature is reached, and further heating is attempted, the appropriate numbers of molecules (in the ratio of 58 to 42 in this case), already in contact at the interface, join to form a new liquid phase, which for the moment is the eutectic solution.
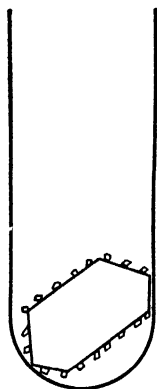
A sharp observer may now notice a moist appearance on the surface of the camphor crystal. However, the melting process does not seem to continue without further rise in temperature. Actually the cessation of melting is due to the exhaustion of solid naphthalene, which was originally present only in scant quantity anyway.

Solid camphor is now in equilibrium with the small superficial coating of eutectic liquid. Let the temperature be now raised by 1°. The activity (or vapor pressure) of the solid is increased more than that of the liquid; therefore the solid now proceeds to melt faster than the liquid solidifies. But the melting dilutes the eutectic liquid with camphor, promptly raising the partial pressure of that component in conformity with Raoult's law. This promptly counteracts the melting process, and a new equilibrium is reached at the higher temperature. Further increases in temperature will cause more and more melting until finally the solid camphor is exhausted; that is, until the material is all in the liquid state. Obviously the final melting point—the only really significant melting point of the mixture in question—cannot be as high as 179°, but it may approach that figure if the original fraction of impurity was small.

Fig. 6.
Melting-Point Tube

The melting range thus really extends from the eutectic temperature up to the point of disappearance of the last crystal. In actual practice, with small amounts of impurity, it is usually impossible to detect the initial melting or eutectic condition. The crystals may not be arranged over the surface of a conspicuous
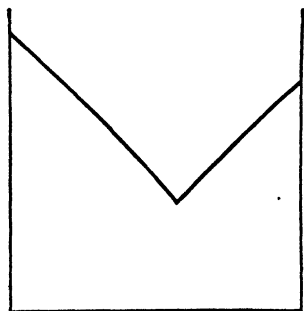
Fig. 7.   Conventional Melt-   Fig. 8.   The System Benzene—
    ing Point Diagram   p-Bromonitrobenzene
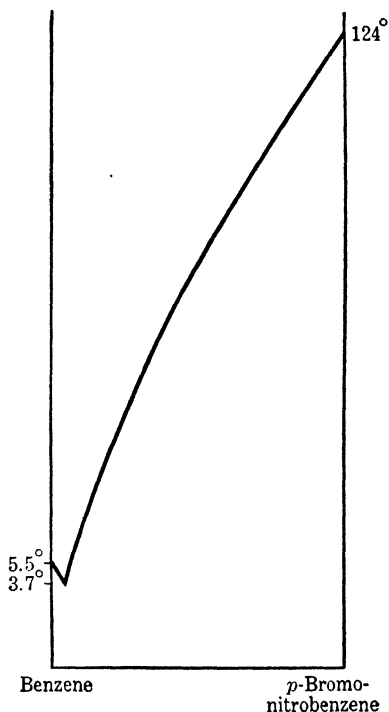
crystal as in the ideal illustration proposed above. Thus the temperature may rise many degrees above the eutectic temperature before an appreciable accumulation of liquid occurs. In the case of camphor contaminated with much naphthalene, one might detect initial melting at 80° or 100°, and would then expect a protracted range of melting. On the other hand, if the initial melting seemed to occur at 177°, the whole process would be complete

within a few tenths of a degree, and the preparation adjudged to be nearly pure. If two workers tested the same impure preparation, one might find a higher *initial* melting temperature, but they should both find the same *final* melting point.

On the melting point-composition diagram of naphthalene and camphor are represented two mixtures, *A* and *B*, which ostensibly have the same melting point, introducing possible confusion. These are readily distinguished by mixing pure naphthalene with each. In case *A* the melting point is lowered; in *B* it is raised.

155. The practical summary of the above discussion is this: a relatively pure preparation has a *short* and *high* melting range; an impure preparation has a *long* and *low* range.

Because of its small molecular weight, water has the tendency to depress the melting points of preparations greatly. Efficient drying is thus desirable.

156. Some substances undergo an abnormally great depression of melting point with addition of the second component. Camphor is of such character. It is accordingly used to advantage as a solvent in the well-known Rast method of determining molecular weight. (See § 211.)

157. If the melting-point depression is of ordinary magnitude and the melting points of two components in a mixture are not very far apart, a melting-point curve of conventional type may be expected, as in Fig. 7. In such a graph the eutectic point is likely to be at some distance from either composition axis. On the other hand, where great difference in melting point exists, the eutectic point may be displaced to an extreme position at one side. An example is seen in the diagram of benzene and *p*-bromonitrobenzene, shown as Fig. 8.

158. "Mixed Melting Points." This incoherent expression, colloquially used in the laboratory, refers to an important application of the foregoing principles to identification of organic compounds. A concrete example is the following:

A research worker has just prepared a compound *X* which he thinks may be *o*-fluorobenzoic acid (m. pt. 122°). There are, however, several other compounds with approximately the same melting point, including benzoic acid itself. Roughly equal weights of *X*

and of known pure o-fluorobenzoic acid from another source are thoroughly mixed, and the melting point of the mixture determined. If X really is the fluoro compound, as suspected, no fall in melting point will be observed. If, however, it happens to be simple benzoic acid, or any compound other than o-fluorobenzoic acid, a sharp change in melting point will probably be observed, with the following possibilities:

(*a*) A drop of several or many degrees if the two compounds do not react with each other.

(*b*) A rise if the two combine to form a new compound of higher melting point.

The foregoing discussion is largely based on the relatively simple assumption that the two compounds in a given mixture are not mutually soluble in the solid state. Unfortunately many substances do not strictly follow the ideal curves pictured. Such abnormalities do not, after all, interfere with the general principle of melting-point depression. Further details are described in special works of the type of Findlay's *Phase Rule*.

Questions

1. How might you find the molecular weight of a substance by determination of melting point?

2. Which would have the lower melting point, a 1% solution of ethyl alcohol in acetic acid, or a 1% solution of water in acetic acid?

3. Suppose you heated a quantity of a pure crystalline substance at a steady rate, introducing just one calorie per minute, until the melting point was passed. If the various temperatures attained were plotted against the number of minutes' time elapsed, what would be the general appearance of the curve so drawn? Of what use might such a curve be?

4. Devise a scheme for determining the melting point of a substance which is so unstable at elevated temperatures that it decomposes before the melting point can be reached in the regular micro procedure.

5. Find the molecular weight of a substance in a case where a mixture of 1 g. of the compound with 100 g. of camphor melts at 172°. (See § 211.)

6. Suppose the substance A (m. pt. 60°) combines quantitatively with an equimolal amount of B (m. pt. 85°) to form a compound AB (m. pt. 160°). Outline the approximate form of the melting-point-composition curve for all possible mixtures of A and B.

7. Why is it easier to determine the melting point of a substance of high heat of fusion than one of low heat?

CHAPTER 13

Recrystallization from Solution

159. When a hot, concentrated solution of an organic compound is cooled, crystals of the compound are expected; but if the melting-point-composition diagram of the system is not considered at least in an approximate practical way, the crystals may consist of the solvent instead of the desired preparation. Such a misfortune is more likely to occur with low-melting compounds of relatively high solubility.

The process of dissolving a substance in a solvent is after all a special case of the melting of the substance in the presence of an "impurity." The solvent is the impurity, which according to rule lowers the melting point of the substance. Hydroquinone, for example, melts at 170°; but in the presence of a suitable excess of water it melts—that is, dissolves—at 80°, 40°, or other relatively low temperatures.

160. Acetic Acid. Avoidance of the blunder cited in § 159 is illustrated by Fig. 1, showing melting points for the system acetic acid-water. The aim of the experiment is the preparation of pure acetic acid by crystallization of that compound from water as solvent. The material at hand consists of a 90% pure acid, assumed herewith to contain water (10%) as its only impurity. Beginning at room temperature, the point A is then located on Fig. 1 as the graphic starting point for a study of behavior upon cooling.

Solution A is cooled, and the vertical arrow AC graphically indicates the first stage of that operation. But C (3° C.) is the so-called freezing point of a 90% mixture. Given time, or the aid of a seeding operation, crystals of pure acetic acid will now separate as the temperature continues to fall. Since the solution is being robbed of acetic acid, the graphic path no longer goes directly downward, as with AC, but bears to the right, as in CE. Before the eutectic point E is reached ($-27°$), the operator filters the mixture obtain-

ing a substantial yield of the desired pure crystalline acetic acid.

A second experiment shows faulty technique in the use of a mixture whose composition is marked on the wrong side of Fig. 1. A 20% solution of acetic acid is cooled from room temperature (B) to $-7°$ (D). At D crystals appear, and a large crop of beautiful material is collected along the course DE, analogous to the crystalliza-
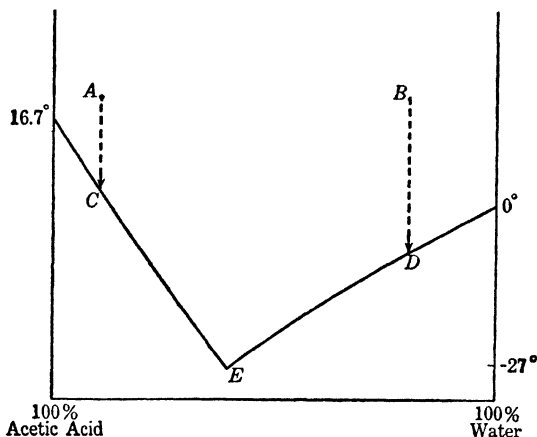
Fig. 1. *Melting Points of Acetic Acid-Water Mixtures*

tion CE above cited. Unfortunately the crystalline product is ice, not acetic acid, and the principles involved in its appearance are quite like those given above in the AC case. One should note, therefore, that crystallization of a given compound may not be successfully accomplished unless the experimenter chooses a solution in which the concentration of the desired substance is in excess of the eutectic concentration. Otherwise he gets either crystals of the solidified solvent, a solid eutectic mixture, or no solid matter at all, as the case may be.

In the case of acetic acid and water the process of crystallization is simple because the two components are miscible in the liquid state in all proportions even at low temperatures. When the mutual solubility of the solute and solvent is limited, a new trouble enters.

161. Separation of an "Oil." Attempts to recrystallize certain compounds result in the appearance of so-called oils, which retain

impurities and confuse inexperienced workers.   Acetanilide and water afford a good example of such troubles, as graphically portrayed in Fig. 2.   The simple cooling of a boiling, saturated aqueous solution of acetanilide first causes the separation of the oil; later the
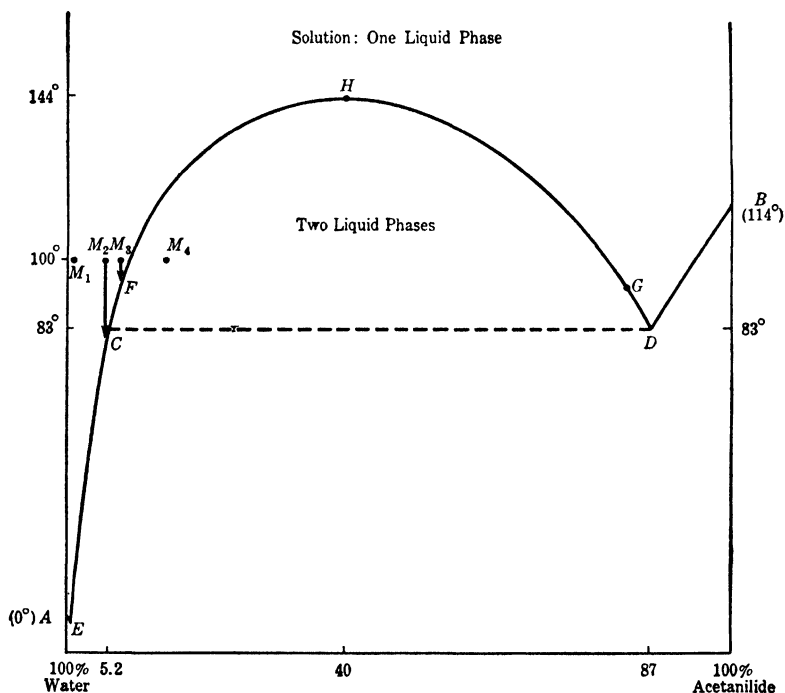
Fig. 2.   The System Acetanilide-Water

oil seems to freeze in a compact mass of questionable purity; finally a terminal yield of relatively pure crystals of acetanilide is obtained from the residual aqueous solution.

In Fig. 2 the melting-point curve starts as usual with the normal melting point of the pure solvent (water) as marked at A, or 0°. As usual it drops to the eutectic E, which in this case happens to be very close to the left vertical axis of the graph.   The right branch of the curve rises from E and normally would proceed to B, the melting point of pure acetanilide.   This curve is broken, however, into two disconnected sections EC and DB.   The intruding inter-

mediate zone *CDGHF* is a field in which acetanilide and water are not miscible. It is impossible to prepare a solution of these two components with any temperature and corresponding concentration falling within that zone. This fact is likely to disturb the process of recrystallization seriously.

Suppose several mixtures, M_1, M_2, M_3, M_4, be made of solid acetanilide with boiling water, with the purpose of finding a suitable solution from which crystals may be obtained upon cooling. Since the mole percentage of solute in each of these mixtures is low, their boiling points will all be just slightly above 100°.

Not all of the mixtures are satisfactory for production of crystals. M_1, for example, is too dilute. Like the acetic acid mixture *B* in Fig. 1, it will yield ice upon extreme cooling. The very short curve-segment *AE* will be involved in such a procedure.

M_2, a 5% solution, in many respects is ideal for recrystallization. As the solution is cooled, a point just below *C* is soon reached, and from thence to *E* a continuous crystallization of the one substance acetanilide will occur. In actual practice such a procedure gives beautiful snowlike crystals, especially if the cooling be done rapidly.

Suppose the worker is dissatisfied with the relatively dilute and possibly voluminous solution M_2, and increases the concentration to 7%, as at M_3. Since M_3 is in the "solution" field, there is still but one phase present in the boiling mixture. M_3 is now cooled to *F*, and threatens to pass into the forbidden zone. Further lowering of temperature forces solution M_3 to eject the excessive amount of acetanilide, which it can no longer hold, together with a small amount of water, in the form of a new separate liquid phase. The point *G* is marked to show the composition of this new liquid phase. Similarly, if the experimenter had chosen some other solution than M_3 between the limits of 5.2 and 40% acetanilide, he would have encountered the two-phase zone at some other point between *C* and *H* on the rising curve; and at such point a corresponding second liquid phase, or "oil," would have appeared with designation at the corresponding point on curve *HGD*.

The new liquid or "oil" phase *G* appears at the outset all through solution *F*, first as a turbid, emulsified suspension; but the droplets of *G* soon coalesce into a pool which falls to the bottom of the crystallizing vessel.

As the mixture of solution *F* and oil *G* is cooled, each phase be-

comes supersaturated with the component which is present in the smaller proportion. F then releases some of its acetanilide, and G gives up some of its water. F becomes C—cooler and less rich in acetanilide; G becomes D—cooler and richer in acetanilide.

At 83°, the temperature of C and D, the zone of crystallization is just reached. C now begins to produce crystalline acetanilide instead of the oil. Being thus stripped of acetanilide, it withdraws a new supply from the oil D. Theoretically this double process should now go on until the oil has all disappeared; that is, D dissolves in C, and then pure acetanilide drops from C.

In practice, however, D usually lies as a compact pool of liquid, and does not get a chance to go through the two theoretical paths. Actually it seems to solidify just as it lies, forming a cake of more or less crystalline material from which the dissolved impurities did not have a good opportunity to escape.

M_4 is worse. Since a solution of M_4 specifications is impossible without operation under pressure, the laboratory worker notices as he boils the M_4 mixture (at about 100°) that the oil is present from the start. Cooling of this mixture gives results just as described for M_3.

The simplest remedy for the difficulties of M_3 and M_4 is of course to dilute the mixture to such a value as M_2, which upon cooling will be certain to miss the line CF.

The dilution plan of course has one drawback. The increase in amount of water involved in the shift from M_3 or M_4 to M_2 means a definite additional loss of acetanilide in the ultimate mother liquor.

To avoid this loss, let solution M_3 be cooled directly without dilution. The oil G of course appears when the main solution reaches the state F; but at this point the mixture is vigorously agitated. When states C and D are reached by the solution and oil, respectively, the emulsion of the two starts to solidify. As before C yields crystals, and D in turn dissolves in C. Since no pool of oil is allowed to accumulate, the formation of crystals may take place freely out in the open. Impurities are easily squeezed out of the separate tiny droplets as they disappear. As soon as the oil D is exhausted, so that only crystals and solution remain, the temperature may now fall. Crystals continue to accumulate, but the agitation is of course no longer necessary.

In general, these difficulties may be expected with low-melting

compounds not extremely soluble in the solvent used. Occasionally one may avoid the whole two-liquid-phase situation by adding a second solvent. (See § 202 (*b*).)

The above phenomena are exhibited to good advantage by the substance succinonitrile ($NC.CH_2CH_2.CN$). Schreinemakers [*Z. physik. Chem.* **23,** 429 (1897)] has given a comprehensive explanation of this case, and Findlay (text, *Phase Rule*) has given a good summary of the original research of Schreinemakers.

CHAPTER 14

Sublimation

162. When an organic preparation is condensed to the liquid state in the normal process of distillation, it is likely to carry with it impurities which are soluble in the distillate. If, however, the product could be deposited directly in the solid state, gaseous impurities would probably be excluded mechanically, since they have little or no opportunity to penetrate or dissolve in a solid mass. In practice the substance is first vaporized, and the vapor is made to pass directly into the solid state without intermediate passage through the liquid state. This process is known in chemical laboratories as "sublimation," and the product is often termed a "sublimate."

In the formal literature of physics and physical chemistry, sublimation is defined more narrowly as the mere passage of a substance directly from the solid to the vapor state. No restoration of the solid is considered. In practical chemistry, however, the mode of vaporization in the operation of sublimation is of secondary importance. The outstanding feature of the process is the short cut from vapor to solid.

In the laboratory, sublimation is often carried out by the heating of a preparation between two watch glasses or two beakers placed mouth to mouth. The vapors expelled from the lower of the two glasses or beakers reach the upper, on whose cool glass surface they form sublimed crystals. This procedure is simple and effective for very small amounts of product, but is tedious where a considerable yield is required. In the preparation of pure anthracene (§ 198) the process is expedited with the aid of a current of air.

Comparatively few organic compounds are well adapted to the process of sublimation. For illustration, three substances of very different adaptability are contrasted as follows: hexachloroethane, readily sublimed, naphthalene, sublimed only with special precautions, and *p*-nitrobenzaldehyde, which practically speaking can-

not be sublimed at all. Figures 1 and 2 illustrate the phenomena.

(a) *Hexachloroethane.* As usual, the vapor-pressure curve of the solid (Fig. 1) is steeper than that of the liquid form; but in this case
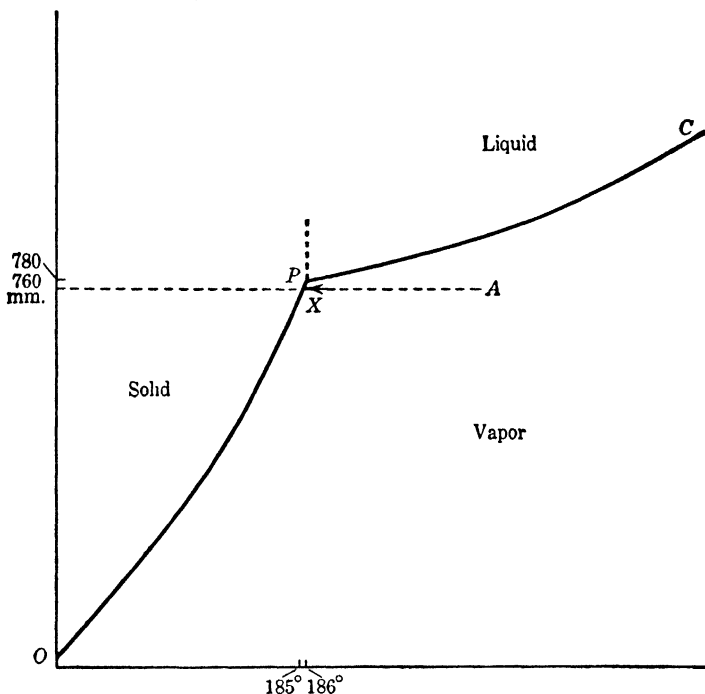
Fig. 1.   Sublimation of Hexachloroethane

the vapor pressure of the solid rises to the remarkable height of 780 mm. before the crystals melt. If the compound is heated above 185°, its vapor pressure tends to exceed 760 mm. An outpouring of vapor, in principle suggestive of boiling, occurs at once, and the solid quietly disappears. The rest of the solid vapor-pressure curve *XP* and the whole liquid curve *PC* are not determinable unless the material is confined in a vessel where the pressure may be elevated. It is thus not possible in the open air to reach points *P* or *C*. If the vapor produced at *X* is further heated, it can only expand at constant pressure, as represented along the dotted line, perhaps to such a point as *A*. The material is now ready for the really significant reverse operation.

Vapor A is cooled, and reaches the status marked at X. At this point vapor is transformed to solid, out of reach of any possible liquid state. Further cooling sharply reduces the vapor pressure of the solid, and the product continues to sublime over the path X to O.

(b) *Naphthalene.* When this substance is heated in a manner
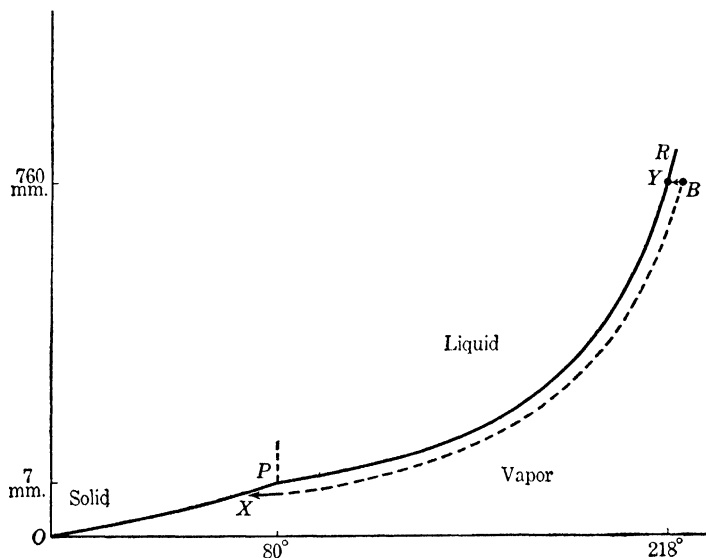
Fig. 2. *Sublimation of Naphthalene*

similar to case (a), the whole distance OP (Fig. 2) is traversed with a climb in vapor pressure to the value of only 7 mm. The compound melts, and not until the distant point of 218° is reached could the whole mass of a substantial amount of the compound go over into vapor. Slight superheating again occurs, yielding a vapor B analogous to A in Fig. 1. When vapor B is cooled, the *liquid-vapor* equilibrium line PR will be encountered. Condensation to the liquid state occurs at Y. Next the temperature will fall to the freezing point P (80°) and the vapor pressure to 7 mm. Since 7 is far below 760, it is thus only a partial vapor pressure, representing a small amount of naphthalene diluted in a large proportion (753 mm.) of air. Most of the naphthalene has already been distilled over the path YP, and thus only a small end product (P to O) will be obtained as a sublimate.

If the operator insists on really subliming the whole mass of naphthalene, he may reduce the pressure by mechanical means, and then reduce the temperature. Both pressure and temperature may be reduced simultaneously as long as the former is kept constantly below the value required to form a liquid phase. The dotted line *BX*, diverted so as to escape contact with the liquid-vapor equilibrium curve, shows the course by which liquid condensation is avoided. It may approach as closely as possible, without harm, provided it does not touch the boundary of the liquid field.

The above result may be accomplished without evacuation of apparatus by mixing the vapor of the desired substance with air or other relatively inert gas. Such dilution lowers the partial pressure of the substance and also cools the material. As a result, a deposit of sublimed crystals accumulates in the cooling chamber, perhaps falling like snow. Such preparations as zinc dust and flowers of sulfur may be made in such a manner. Great care should be taken not to allow a flame to reach a subliming chamber in which finely divided combustible organic matter is suspended in air. Serious accidents, analogous to the well-known dust explosions of flour mills, have occurred in such situations.

(*c*) *p-Nitrobenzaldehyde* has a vapor pressure of 0.009 mm. at 100°, a temperature slightly below its melting point. It is impracticable to produce a useful quantity of solid crystals from so rare a vapor. Many substances of common use have vapor pressures much under 1 mm. at their melting points, and thus are not well adapted to sublimation. Among these one would expect to find many of the impurities whose elimination is sought. Since they do not sublime, they do not interfere with purification of those substances which do sublime.

In research it is sometimes desirable to sublime a substance of the (*c*) type, necessitating operation at greatly reduced pressure. Large connecting tubes or passageways are needed so that the rarefied vapors may pass
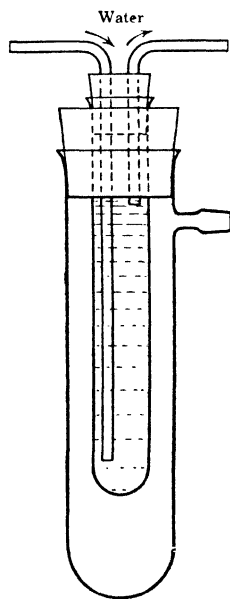
Fig. 3. *Sublimation in Vacuo*

through in sufficient volume to permit a reasonable velocity of sublimation. The effect of a wide passageway is also attained by placing the condensing surface in the boiler itself, close to the substance being sublimed. The inner member (Fig. 3) may then be lifted out carefully with its adhering burden of sublimate, occurring often as feathery crystals.

163. Frozen Mist. Genuine sublimation of an ordinary organic
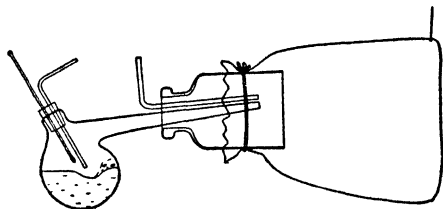
Fig. 4. Pseudo Sublimation

compound, whose vapor pressure in the solid state seldom is as high as 10 mm., is bound to be slow. One may then resort to the "frozen-mist" process, which may be called "pseudosublimation." For example, benzoic acid is melted in a retort and heated to about 170°. Air is blown through the liquid, carrying quantities of benzoic acid vapors to the cooling chamber, which is a cloth bag attached much like the bag of a vacuum cleaner. As the diluted vapor reaches the bag and is slightly cooled, it condenses to a liquid, being above its melting point (122°) and below its boiling point (249°). This liquid first occurs as a fine mist, or suspension of minute droplets of liquid in the air. Before the mist has a chance to coalesce into large drops of distilled liquid, it meets a current of refrigerated air blown into the bag. The fine droplets immediately solidify. Any impurities of a volatile nature which might for the moment have been dissolved in the droplet are squeezed out in the crystallization and blow away. Accordingly the "pseudosublimate" may be just as pure in the end as a genuine sublimate which did not pass through the liquid state. It is likely that some of the commercial "sublimed" products actually come from pseudosublimation.

164. The accompanying table shows how great are the differences in the vapor pressures of various substances at their melting points.

	Vapor Pressure	*Melting*
Substance	*at Melting Point*	*Point*
Carbon dioxide	3900 mm.	$-57°$
Hexachloroethane	780 mm.	$186°$
Phosphorus pentachloride	760 mm.	$166°$
Camphor	370 mm.	$179°$
Nitrogen	96 mm.	$-210°$
Iodine	90 mm.	$114°$
Ammonia	45 mm.	$-78°$
Benzene	36 mm.	$5.5°$
Naphthalene	7 mm.	$80°$
Benzoic acid	6 mm.	$122°$
Water	4.58 mm.	$0°$
Bromine	0.44 mm.	$-7°$
Zinc	0.15 mm.	$419°$
Sulfur	0.03 mm.	$119°$
p-Nitrobenzaldehyde	0.009 mm.	$106°$
Toluene	0.001 mm.	$-95°$
Mercury	0.000001 mm.	$-39°$

Questions

1. Describe the procedure you would expect to use if you were required to purify the following substances by sublimation:

(*a*) camphor;   (*b*) sulfur;   (*c*) benzene.

2. Suppose the iodobenzene cited in the steam-distillation experiment of § 83 were replaced by camphor. Describe the probable behavior of the system when the attempt is made to conduct the steam distillation.

3. What advantages might there be in "steam sublimation" as contrasted with ordinary sublimation in air?

4. At least three of the substances mentioned in the *upper part* of the foregoing vapor-pressure table are used for killing or repelling insects. What relation might this fact have to the subject under discussion in this chapter?

5. On the basis of principles discussed in this chapter, explain the peculiar behavior of liquid carbon dioxide when released in quantity from a cylinder into a cloth bag.

CHAPTER 15

Organic Acids and Bases

165. Many operations of organic synthesis, particularly those used in Chap. 16, depend upon the conversion of organic acids or bases into salts, or the reverse. Unfortunately the time-honored definitions of acids and bases are not satisfactory in the organic field, and thus certain newer conceptions are in order.

An acid is a compound which is capable of giving up protons (positively charged atoms of hydrogen) *to a base which it may encounter.* No free circulation of isolated "hydrogen ions" is recognized.

A base is a compound which is capable of accepting protons from an acid. No necessity of hydroxyl ions is recognized. Hydroxyl ion is merely a special case of a base in the inorganic domain, and there are thousands of other bases, of entirely different constitution, among organic compounds.

Probably the most important single characteristic of either an acid or a base is its **strength.** Since knowledge of relative strengths of various organic acids comes from the behavior of these acids with bases, it is perhaps best to examine first the chemistry of basic substances.

166. Bases. Hydroxyl ion, OH^-, is the commonest and most important base. The fact that some metallic or metal-like constituent is usually associated with hydroxyl leads to the common habit of calling the two together a base—for example, sodium hydroxide. Actually the real base is the hydroxyl part alone, with only secondary influence from the sodium. Its chemical reactions require no "hydrogen ion," but are rather illustrated as follows:

$$OH^- + CH_3COOH \rightarrow H_2O + CH_3COO^-$$
Hydroxyl ion + acetic acid → water + acetate ion
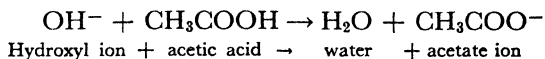
As usual with a base, hydroxyl takes a proton from the acid. Similarly, other ionic bases, such as carbonate, CO_3^-, phosphate,

$PO_4^{\equiv}$, and borate, $BO_3^{\equiv}$, could be used with varying degrees of efficiency in place of hydroxyl.

In organic chemistry, however, most of the well-recognized bases are not negative ions, but electrically neutral substances in complete molecular form. The most important of these are structurally similar to ammonia. Ammonia itself, for years awkwardly called a "base-former," is simply a base, as illustrated in the following well-known reaction, conducted in the absence of water:

$$NH_3 + HCl \rightarrow NH_4^+ + Cl^-(\rightarrow NH_4Cl)$$
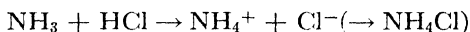
Organic amines play a similar role, such as that of aniline when treated with hydrogen chloride:

$$C_6H_5NH_2 + \quad HCl \quad \rightarrow C_6H_5NH_3^+ + Cl^-$$

Aniline   Hydrogen chloride   "Aniline hydrochloride"
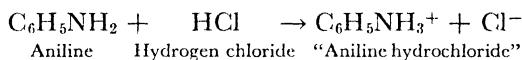
The laws of simple valence give no clear explanation of the above reactions. If the Lewis electronic formulas are used, however, the procedure seems to be more logical.

$$\begin{array}{cc}
\text{H} & \text{H} \\
\text{H}:\ddot{\text{N}}: & (C_6H_5):\ddot{\text{N}}: \\
\ddot{\text{H}} & \ddot{\text{H}} \\
\text{Ammonia} & \text{Aniline}
\end{array}$$
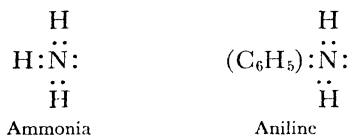
In such a formula a single bond is assumed to be a pair of electrons serving the purpose of holding together the various positive nuclei N, C, H, which would otherwise repel each other. In the molecule of aniline, as well as that of ammonia, there is an extra pair of electrons not shared by hydrogen. Apparently every amine base has such an unshared pair of electrons. Plainly there exists an opportunity for the base to attract a proton, which may thus be drawn out of an acid and brought over to share the extra electron pair. Rewriting the last equation in the Lewis form:

$$\begin{array}{ccc}
\text{H} & & \text{H} \\
(C_6H_5):\ddot{\text{N}}: + \text{H}:\ddot{\ddot{\text{Cl}}}: & \rightarrow & (C_6H_5):\ddot{\text{N}}:\text{H}^{(+)} + :\ddot{\ddot{\text{Cl}}}:^{(-)} \\
\ddot{\text{H}} & & \ddot{\text{H}}
\end{array}$$
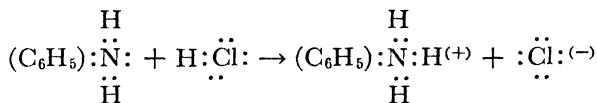
The resulting aniline hydrochloride is sometimes represented by the expression

$$C_6H_5NH_3^+........Cl^-$$
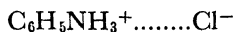
in which the dotted line shows a polar attraction and not a true chemical bond.

The requirements of a base are two: first, an unshared pair of electrons; second, an inherent tendency to attract protons at the expense of an adjoining acid. If that tendency of attraction is great, the base is considered strong. If the attraction is slight, the base is weak.

Similar adjectives are applied to acids. If, however, the acid gives up its protons with relative ease, it is called a strong acid; if it holds protons tightly, it is weak.

Actual measurement of the strength of an acid requires the use of a standard weak base as a reference reagent. Similarly the strength of a base is found by testing the compound with some standard weak acid. Water, which is both a weak base and a weak acid, is used for both kinds of measurement. For example, the strength of ethylamine could be found by testing the ability of this organic base to take protons from water:

$$C_2H_5NH_2 + H_2O \rightleftharpoons C_2H_5NH_3^+ + OH^-$$
Ethylamine   Ethylammonium ion
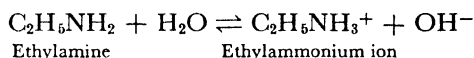
It is important to notice that this reaction runs to equilibrium, and does so almost instantaneously. At equilibrium only a limited fraction of the organic base is found combined with protons in the ethylammonium form. The strength of the base is denoted by the extent to which the transfer to the $C_2H_5NH_3^+$ form has occurred at equilibrium.

Ignoring the concentration of water in this equilibrium, which is practically constant, an equation may be set up in conformity with the law of mass action. In this equation brackets refer to concentration; for example, [OH$^-$] means "concentration of hydroxyl ion":

$$\frac{[C_2H_5NH_3^+] \times [OH^-]}{[C_2H_5NH_2]} = K_B$$

which is known as the **ionization constant** of the base.

In the table given in § 167 a few representative bases are listed. Bases like ethylamine, with constants in the vicinity of 10^{-3} to 10^{-4}, would be regarded as rather weak in inorganic chemistry, by contrast with hydroxyl ion, a powerful base. Only 1 to 5% of the base accepts protons in common water solutions. In the organic field,

however, a constant of 10^{-3} indicates a relatively strong base. Aniline, with a K_B of 4.6×10^{-10}, is typical of a weak base. In a saturated aqueous solution of aniline only a very small fraction of 1% of the aniline molecules accept protons from water.

167. Acids. With acetic acid as an example, water is again drafted into service as a substance for reference—this time to play the role of a **base**:

$$H_2O + CH_3COOH \rightleftharpoons H_3O^+ + CH_3COO^-$$
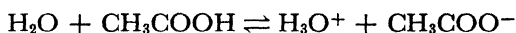
Again discarding the concentration of water as a useless constant:

$$\frac{[H_3O^+] \times [CH_3COO^-]}{[CH_3COOH]} = K_A$$

known as the **ionization constant** of the acid.

In this case the constant is recorded (see following table) as 1.8×10^{-5}. This is a median value in organic chemistry, and indicates that acetic acid is an acid of moderate strength. Hundreds of ordinary carboxylic acids are found in this class, with constants from 10^{-4} to 10^{-5}. Those acids whose K_A value is in the range of 10^{-1}

IONIZATION CONSTANTS

Acids		*Bases*	
Trichloroacetic acid	2×10^{-1}	Guanidine	3×10^{-1}
Dichloroacetic	5×10^{-2}	Dipropylamine	1.02×10^{-3}
Oxalic (first H^+)	3.8×10^{-2}	Diethylamine	1.26×10^{-3}
Chloroacetic	1.6×10^{-3}	Ethylamine	5.6×10^{-4}
Lactic	1.4×10^{-4}	Triethylamine	5.3×10^{-4}
Benzoic	6.6×10^{-5}	Ammonia	1.8×10^{-5}
Acetic	1.8×10^{-5}	Strychnine	1×10^{-7}
Carbonic (first H^+)	3×10^{-7}	Pyridine	2.3×10^{-9}
Phenol	1.3×10^{-10}	Aniline	4.6×10^{-10}
Sucrose	1.8×10^{-13}	Dimethylaniline	2.4×10^{-10}
Water	10^{-16}	α-Naphthylamine	9.9×10^{-11}
Ethyl alcohol	10^{-18}	o-Chloroaniline	9.2×10^{-13}
Phenylacetylene	10^{-21}	Urea	1.5×10^{-14}
Triphenylmethane—not over	10^{-33}	Water	—
Diphenylmethane—not over	10^{-35}	Acetamide	—
Phenylmethane (toluene)	—	Triphenylamine	—
Methane	10^{-43}	Acetone	—

to 10^{-3} are rated as strong. This statement infers that a large fraction of the molecules of such strong acid are found to have reacted with water in their equilibrium mixture with that solvent. Those acids with constants of 10^{-10}, or thereabouts, exist largely in their original molecular form in the water equilibrium and are called weak. Constants of extremely low values, such as 10^{-20} to 10^{-43}, apply to substances scarcely recognized as acids in common chemical operations. They are not derived from precise measurements, but instead are the result of hypothetical assumptions.

Hydrogen chloride is so strong an acid that it yields its protons to water completely—at least in ordinary solutions:

$$H_2O \ + \ HCl \ \rightarrow \ H_3O^+ \ + \ Cl^-$$

$$\overset{\displaystyle H}{H:\overset{..}{\underset{..}{O}}:} \ + \ \overset{\displaystyle H}{H:\overset{..}{\underset{..}{Cl}}:} \ \rightarrow \ \overset{\displaystyle H}{H:\overset{..}{\underset{..}{O}}:H^{(+)}} \ + \ :\overset{..}{\underset{..}{Cl}}:^{(-)}$$
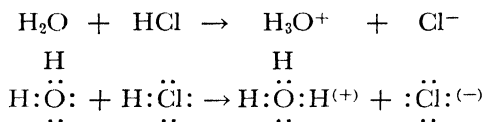
The resulting ionic pair $H_3O^+Cl^-$ is known as an **oxonium salt,** analogous to ammonium salts, although the laboratory label probably reads "Hydrochloric Acid, HCl, Dilute." The H_3O^+ ion itself is sometimes called "hydronium ion," again with analogy to the ammonium ion.

Neutralization of an organic base by a strong acid in water solution calls for consideration of the H_3O^+ ion. For example, suppose aniline is allowed to react with dilute aqueous hydrochloric acid instead of pure hydrogen chloride. H_3O^+ now serves as the acid:

$$C_6H_5NH_2 + H_3O^+Cl^- \rightarrow C_6H_5NH_3^+ + Cl^- + H_2O$$
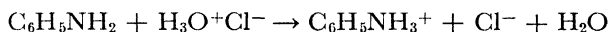
This equation simply means that the nitrogen base, like most of its kind, is stronger than an oxygen base like water. Therefore it almost completely strips the oxonium ions of their extra protons, releasing ordinary water molecules.

168. Extremely Weak Bases. An organic base which is weaker than water cannot be detected as a base in water solution. For illustration, suppose aqueous hydrochloric acid were used in an attempt to react with triphenylamine, an extremely weak base. Unfortunately this amine, being weaker than water, will be unable to take protons from H_3O^+. It thus appears to be inert and neutral. In this manner literally thousands of very weak organic bases often escape identification as bases. These include ethers, which do not

react appreciably with dilute hydrochloric acid, but react readily with anhydrous HCl:

$$\text{R:}\ddot{\text{O}}\text{:} + \text{H:}\ddot{\text{C}}\text{l:} \rightarrow \text{R:}\ddot{\text{O}}\text{:H}^{(+)} + \text{:}\ddot{\text{C}}\text{l:}^{(-)}$$
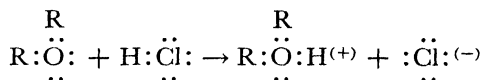
Sometimes these "ether-oxonium salts" may even be recrystallized.

169. Extremely Weak Acids. An organic acid which is weaker than water cannot be "neutralized" in water solution. Water simply gives up its protons more readily than the weak acid, leaving the latter untouched in spite of the possible addition of large amounts of bases. Practical applications of this principle will appear later.

170. Practical Applications. From the above numerical data and theory a number of practical applications are derived, as follows:

(a) *Ordinary carboxylic acids*, containing carbon, hydrogen, and oxygen only, are so much weaker than the common strong inorganic acids such as hydrochloric and sulfuric that they may readily be produced from their salts by mere admixture of the latter with the strong acid. Water does not appreciably interfere with this process, since the oxonium ion H_3O^+, which holds the acidic protons in aqueous solutions of strong acids, is itself a stronger acid than the carboxylic acids which are to be formed. If the desired carboxylic acid is to be isolated by distillation, sulfuric acid, a nonvolatile reagent, is employed, so that any excess of the reagent will not be distilled. On the other hand, if the organic acid is to be isolated by crystallization, hydrochloric acid is employed so that any excess will easily be dissipated by simple evaporation.

(b) *Phenols* are so much weaker than carboxylic acids that separations of the former from the latter are occasionally based upon this fact. The mixture of phenol and carboxylic acid is treated with sodium bicarbonate. The carboxylic acid yields its proton to the bicarbonate ion, producing carbonic acid, a weaker acid, while the phenol does not react, since it is weaker than carbonic acid. The unreacted phenol is then isolated by ether extraction, distillation, or other process to which the carboxylic acid, now in the form of its salt, does not respond.

(c) The fact that acids weaker than water may not be neutralized with aqueous bases is turned to advantage in the purification of

ethyl alcohol contaminated with acids. The addition of sodium hydroxide converts into nonvolatile salts all carboxylic acids, all phenols, and, of course, all strong inorganic acids. Barring the presence of neutral or basic volatile substances, a distillate containing only alcohol and water may easily be obtained from the mixture.

(*d*) Closely connected with the foregoing principle is the rule that salts of acids weaker than water must be carefully protected from moisture. Water, the stronger acid, would of course react with such compounds as sodium ethylate, calcium carbide (acetylide), and zinc diethyl. Even salts of acids slightly stronger than water, such as sodium acetoacetic ester, react with water so extensively as to upset synthetic procedures involving those salts. Naturally all such salts are prepared with complete avoidance of water.

(*e*) Compounds of the type of toluene and ethane are so low in acidic strength that their sodium salts are prepared only with elaborate precautions. Furthermore, these salts are so reactive that admixture of moisture or even ordinary air causes violent decomposition and spontaneous combustion. Accordingly they find no application in common organic synthesis.

(*f*) Somewhat analogous to (*a*) above, it becomes evident that a weak organic base may be expelled from its salt by admixture of a stronger base. For example, aniline hydrochloride (§ 292) is converted into free aniline base by the addition of hydroxyl ion (sodium hydroxide):

$$C_6H_5NH_3{}^+ + OH^- \rightarrow C_6H_5NH_2 + H_2O$$
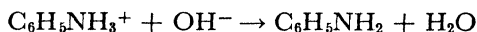
(*g*) Many organic compounds not commonly recognized as bases will form salts with anhydrous acids. Such compounds are too weak to react even with the relatively strong H_3O^+ acid. Given a strong anhydrous acid, like concentrated sulfuric acid, a reaction takes place, and the base dissolves. Advantage is taken of this situation in qualitative organic analysis. (See § 425.) Here cold concentrated sulfuric acid is used to identify oxygen and nitrogen derivatives by observing its power to yield protons to these compounds, thus forming salts which dissolve in the acid. It is probable that concentrated sulfuric acid plays the same role in the well-known acid treatment of petroleum widely employed in refineries. To be sure, such concentrated sulfuric acid is not 100% pure. It may be reported to contain 5 to 8% of water. Such water is of course not free

(basic) H_2O, but is in the form of H_3O^+ or similar coordinated hydrate. The residual acid therefore serves virtually as a non-aqueous reagent and can form salts of ethers, aldehydes, ketones, esters, nitriles, etc.

Structural formulas of these salts offer no fundamental novelty in arrangement. For example,

$$C_3H_7-O-\overset{\underset{\displaystyle \overset{O^+}{\underset{\displaystyle \overset{\diagup\diagdown}{H\quad HSO_4^-}}{\|}}}{C}}-C_3H_7$$

Propyl butyrate
acid-sulfate

Benzophenone
acid-sulfate

$$C_5H_{11}-S_+-C_5H_{11}$$
$$\overset{\diagup\diagdown}{H\quad HSO_4^-}$$

Diamyl sulfide
acid-sulfate
(a "sulfonium" salt)
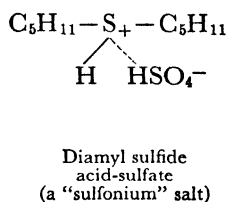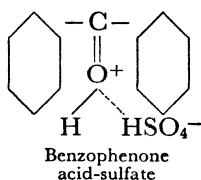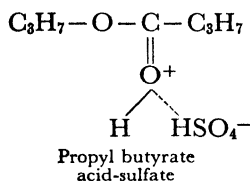
When a compound such as one of the above is poured upon ice (thus avoiding high temperatures in dilution) the aqueous base H_2O, furnished by the ice, immediately reacts with the oxonium or sulfonium salt, expelling the weak organic base, which then separates in liquid or solid form. For example,

$$C_3H_7-O-\overset{\underset{\displaystyle \overset{O^+}{\underset{\displaystyle \overset{\diagup\diagdown}{H\quad HSO_4^-}}{\|}}}{C}}-C_3H_7 \;+\; H_2O \rightarrow \left\{ \begin{array}{l} C_3H_7-O-\overset{\underset{\displaystyle O}{\|}}{C}-C_3H_7 \\[2mm] +\, H_3O^+ + HSO_4^- \end{array}\right.$$
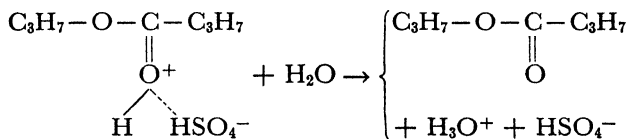
Concentrated sulfuric acid, particularly the anhydrous and fuming grades of the reagent, are known to be excellent for dissolving organic matter which adheres to soiled glassware. It is likely that the largest part of this powerful solvent effect is due to the ability of the anhydrous reagent to convert oxidized matter in the organic stains or tars into salts which are of course very soluble in the sulfuric acid.

(*h*) Salts of extremely weak amine bases may be prepared with the aid of similar principles, but with the use of a convenient diluent. For example, in the molecule of dinitroaminobenzoic acid the basic character of the amine group is suppressed by the accumulated force of three radicals of somewhat acidic character. Anhydrous alcohol, ether, or mixtures of the two are then used as solvents instead of water. Gaseous hydrogen chloride then causes the precipitation of the desired hydrochloride in an effective manner.

CHAPTER 16

Separation of Substances from Mixtures

171. Tests of Laboratory Skill. One of the neatest methods of distinguishing the intelligent student of laboratory practice from the "cookbook" operator deals with ability of the worker to separate individual compounds from mixtures. For example, an examination may include questions like the following:

(*a*) Using any desirable combination of physical and chemical means, how would you isolate pure aniline and pure nitrobenzene from a mixture of the two?

(*b*) How would you prepare pure acetic acid and pure benzene from a mixture of the two?

(*c*) How would you purify *n*-hexyl chloride from a contaminating residue of *n*-hexyl alcohol, the original raw material used in a synthesis of the chloride? (It is assumed that the alcohol need not be saved.)

172. Solution of Problems. (*a*) The mixture is first shaken with an excess of dilute hydrochloric acid. Two distinct liquid phases remain; an aqueous solution of aniline hydrochloride, and under this a layer of unchanged nitrobenzene. The nitrobenzene is separated, washed free of traces of acid, dried, and distilled, with promise of high percentage of recovery. The aniline hydrochloride solution is made alkaline, steam-distilled, extracted with ether; the extract is dried, ether is expelled, and residue of aniline is distilled.

(*b*) The mixture is shaken with an excess of aqueous sodium hydroxide. This completely extracts the acetic acid, converting it into the polar salt. The residual benzene may then be separated, filtered if necessary, dried, and distilled.

The solution of sodium acetate is evaporated to dryness, and the water of hydration expelled by cautious heating of the crystalline residue. Anhydrous (100%) sulfuric acid is now added. Upon distillation, pure "glacial" acetic acid is obtained.

(*c*) The crude hexyl chloride is washed with concentrated sulfuric

acid, which takes out the alcohol as hexyl acid sulfate, or an acid-soluble oxonium salt, as described in § 170 (g). The chloride, being nonbasic, is left behind. It is washed with dilute sodium hydroxide and water, dried with magnesium sulfate or calcium chloride, and distilled.

Problems such as those illustrated above depend largely upon principles discussed in Chap. 15, which should be read in advance. For further practice, two lists of mixtures are given below. The first (§ 173) deals with the problem of separating and purifying two substances, while the second involves merely the purification of the one main component, with rejection of accompanying material. A significant test of proficiency comes from the writing of complete, exact directions for any given separation, suitable for the guidance of a novice. In such directions there should be not only correct application of chemical reactions, but proper choice of apparatus and physical methods.

173. Separation of Two Substances. How would you prepare the individual components, each in a pure state, from each of the following mixtures?

1. Benzoic acid and naphthalene.
2. *p*-Toluidine and *o*-nitrotoluene.
3. Benzoic acid and phenol. (Note that the dissociation constant of benzoic acid is very much greater than that of phenol.)
4. Aniline sulfate and sulfanilic acid. (Change one component into volatile form.)
5. Hexyl alcohol and cresol. (The alcohol is a weaker acid than water.)
6. *n*-Butylamine and *n*-hexane.
7. Benzaldehyde and benzyl chloride. (Convert one component into water-soluble form, from which it is easily reclaimed.)
8. Aniline and dimethylaniline. (Use the fact that dimethylaniline has no $N-H$ chemical bond.)
9. Diamylamine and diphenylamine. (Aromatic bases are weaker than aliphatic.)
10. *tert*-Butyl alcohol and ethyl alcohol. (Note differences in ease of esterification.)
11. Aminobenzoic acid and benzoic acid. (Aminobenzoic acid is amphoteric.)
12. Aminobenzoic acid and aniline.

174. Purification. Frequently but one of the two or more organic substances in a mixture is desired. The problem then permits the virtual destruction or loss of the others, and allows of greater variety of treatment.

How would you purify each of the following without concern about the loss of the accompanying materials?

1. Pentane (containing amylene).
2. Methyl aniline (containing aniline).
3. *n*-Amyl butyrate (containing *n*-amyl alcohol).
4. Ethyl acetate (containing ethyl alcohol and acetic acid).
5. Quinoline, a tertiary amine (containing aniline and phenol; all three substances slightly volatile at 100°). .
6. Methyl ethyl ketone (containing ethyl alcohol).
7. Diethyl ether (containing amylamine, as in "recovered ether" which had been used in an extraction and distilled without thorough purification).
8. Methyl 3,5-dinitrobenzoate (see § 442) contaminated with a residue of 3,5-dinitrobenzoic acid (also solid) left over from an incomplete esterification reaction.
9. *n*-Hexane contaminated with residual *n*-propyl bromide, the substance used in its synthesis by the Wurtz reaction.
10. Di-*n*-butyl ether (containing *n*-octane).
11. Aniline (containing benzylamine).
12. Phenol (containing *m*-xylene).
13. Acetic acid (containing acetic anhydride).
14. Ethyl alcohol (containing acetic acid and aniline).
15. Benzyl alcohol (containing valeric acid).
16. *n*-Octane (containing dibutyl ether).
17. Benzene (containing benzaldehyde).

Part II

LABORATORY EXPERIMENTS

(Note. *Numbers marked "Ref.," in connection with various optional experiments described below, refer to the laboratory manuals listed in* § *175, p. 155.*)

CHAPTER 17

Laboratory Manuals of Organic Chemistry

175. In Part II of this volume frequent reference is made by number to other laboratory manuals, as listed below.

1–22. Adams and associates, *Organic Syntheses*, Wiley, New York, (Accompanying reference numbers also indicate the volume numbers in the Organic Syntheses series.)

23. Adams and Johnson, *Laboratory Experiments in Organic Chemistry*, Macmillan, New York, 1940.

24. Adkins and McElvain, *Practice of Organic Chemistry*, McGraw-Hill, New York, 1933.

25. Cheronis, *Semimicro and Macro Organic Chemistry*, Crowell, New York, 1942.

26. Coghill and Sturtevant, *Introduction to the Preparation and Identification of Organic Compounds*, McGraw-Hill, New York, 1936.

27. Cohen, Julius, *Practical Organic Chemistry*, Macmillan, New York, 1924.

28. Coleman and Arnall, *Synthetic Organic Chemistry*, Blakiston's, Philadelphia, 1926.

29. Colbert, *Laboratory Technique of Organic Chemistry*, Century, New York, 1942.

30. Cumming, Hopper, and Wheeler, *Systematic Organic Chemistry*, Constable, London, 1931.

31. Fieser, *Experiments in Organic Chemistry*, Heath, Boston, 1941.

32. Fischer, Emil, *Preparation of Organic Compounds* (translation from the German), Van Nostrand, New York, 1928.

33. Fisher, Harry, *Laboratory Manual of Organic Chemistry*, Wiley, New York, 1938.

34. Gattermann, L., *Practical Methods of Organic Chemistry* (translation from an early German edition), Macmillan, New York, 1928.

35. Gattermann-Wieland, *Laboratory Methods of Organic Chemistry*

(translation of a recent revised and enlarged German edition), Macmillan, New York, 1937.

36. Heidelberger, *Advanced Laboratory Manual of Organic Chemistry*, Chemical Catalog, New York, 1923.

37. Hickinbottom, *Reactions of Organic Compounds*, Longmans, Green, New York, 1936.

38. Mann and Saunders, *Practical Organic Chemistry*, Longmans, Green, New York, 1936.

39. Norris, *Experimental Organic Chemistry*, McGraw-Hill, New York, 1923.

40. Noyes, *Organic Chemistry*, Chemical Publishing, New York, 1926.

41. Porter, Stewart and Branch, *Methods of Organic Chemistry*, Ginn, Boston, 1927.

42. Richter, *Laboratory Manual of Elementary Organic Chemistry*, Wiley, New York, 1940.

43. Sudborough and James, *Practical Organic Chemistry*, Blackie, Glasgow, 1924.

44. Vanino, *Präparative Chemie*, Vol. II, Enke, Stuttgart, 1923.

45. Wertheim, *A Laboratory Guide for Organic Chemistry*, Blakiston's, Philadelphia, 1937.

EXPERIMENT 1

Preliminary Laboratory Work

Note. *Of the following introductory operations, perform only those specified by the instructor, according to the arrangements of your laboratory.*

176. Inspection of Desk Equipment. First make sure that the laboratory desk contains all of the apparatus specified on the official list. A copy of the list may be obtained from the storeroom if one is not found in the desk. Before making complaint about possible de-

| Distilling flask | Filter flask | Buechner funnel | Adapter | Dropping funnel |

Liebig (water-cooled) condenser

Air-cooled condenser

Addition tube
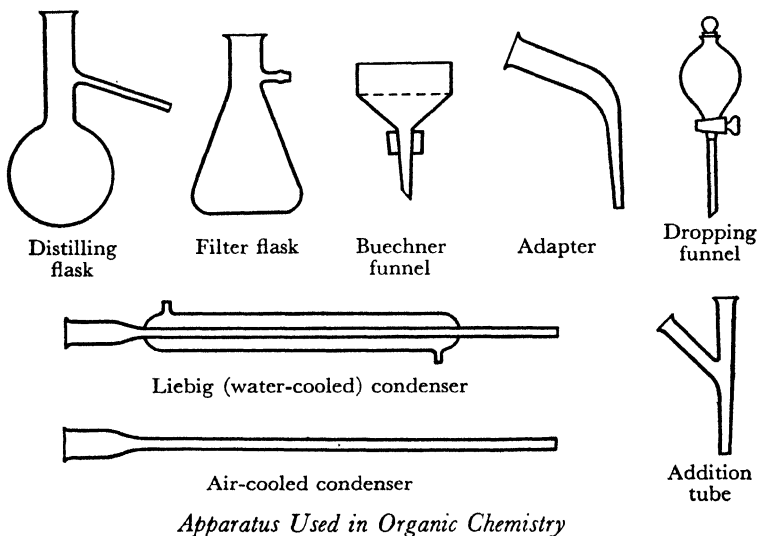
Apparatus Used in Organic Chemistry

ficiencies in desk equipment, examine the entire outfit in detail and bring all troubles to the storeroom at one time. Return defective pieces and obtain any missing articles on the first day of laboratory work. If any piece of apparatus is slightly damaged, but still fully serviceable, you may be instructed to keep it; but you should write a

brief memorandum of such defects on a slip of paper, and have this signed by the storekeeper.

Note particularly the possibility of inconspicuous defects in those of the following pieces which may be on your list:

Water-cooled (Liebig) condenser; watch for concealed cracks in the inner tube at points where the outer tube is attached to the inner.
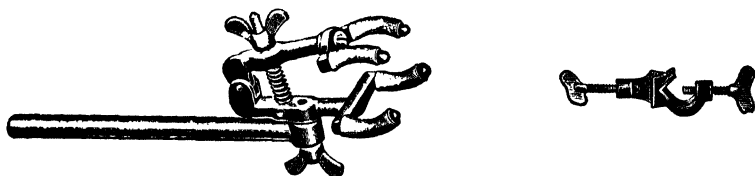
Condenser Clamp and Clamp Holder

Thermometer; if it has been abused by careless cooling in faucet water, it may have inconspicuous cracks near the mercury well.

Gas hose; if used tubing is furnished, beware of rubber which is cracked or has weak spots due to fire damage.

Separatory or dropping funnel; see that the glass stoppers are the ones which belong to the funnel, and which thus fit properly.

177. Broken Glassware. Do not discard broken glassware which may be repaired to advantage by a glass blower. Consult the storekeeper, who will advise you of arrangements for repair service or give credit in exchange for new equipment. For example, distilling flasks and dropping funnels with broken delivery stems are often readily mended.

178. Preparation of Apparatus for the First Experiments. Examine the directions for the first two experiments assigned by the instructor and prepare the necessary glass, rubber, and cork parts for assembly as needed later. Before boring corks for this purpose, read § 15 carefully. If one of the first assignments is the preparation of absolute alcohol, time may be saved by carrying out the directions of § 179 next following.

179. Absolute Alcohol. Start this experiment at once—before assembling equipment for distillation—as described in § 212, and proceed to the point where a delay of two or more days is required. Next read the discussion of the use of a reflux condenser (§ 24), and fit the water-cooled condenser in the proper manner to the flask

holding the quicklime and alcohol, ready for prompt use on a subsequent day.

180. Preparation of Boiling Stones. Read § 47. Break up in an iron mortar 25 to 50 g. of clean, dry unglazed crockery, and pass the granular product through suitable sieves. Crush all of the material to a size not exceeding 5 mm. in diameter, and discard the dust and fine grains under 2 mm. Preserve the pieces of 2 to 5 mm. size as boiling stones, and keep them clean and dry in a bottle. Never wash these stones with water or other liquid. Whenever a liquid "bumps" during distillation or refluxing, interrupt the heating for 2 or 3 minutes and then place three or four stones in the boiler. It is well to develop the habit of adding these stones to all mixtures undergoing distillation, except in reduced-pressure operations. Note the last part of § 47, dealing with a fire hazard in the use of boiling stones.

181. Preparation of Cleaning Solution. Select a Pyrex beaker of 250- to 400-cc. size, and make special note that the vessel does not have the slightest crack. In this beaker, mounted over wire gauze, heat about 100 cc. of technical concentrated sulfuric acid to about 100°. With a glass rod stir in about 3 g. of finely granulated sodium or potassium dichromate. Continuous stirring is essential to prevent the agglomeration of the resulting chromic acid into large masses. Allow the mixture to cool to 50° or below, and pour both the orange-red solution and the precipitated chromic acid into a dry *bottle* (of glass-stoppered type) of about 125- to 250-cc. capacity. Do not use a flask or other thin-walled vessel for storage of cleaning solution. The reagent is capable of setting fire to woodwork, and no risk of breakage should be incurred. The use of this solution is described in § 8.

182. Preparation of Anhydrous Magnesium Sulfate. Spread about 35 g. of Epsom salt ($MgSO_4 . 7H_2O$) in a thin layer in a 4- or 5-inch evaporating dish and heat the dish over wire gauze with a Bunsen burner. The material will partially melt, and nearly half of its mass will be expelled in the form of steam. A dull white, chalky mass should remain as a residue. Crush this into coarse granules and preserve the whole product (granules and powder) in a well-corked wide-mouthed bottle, ready for use as a neutral nonreactive drying agent. See §§ 118 and 125 for further details.

EXPERIMENT 2

Calibration of a Thermometer

183. Determine the accuracy of your high-range thermometer at the 0°, 100°, and 218° points as described below, and test the low-range thermometer at 0° and 100°. Read §§ 18–20.

184. Correction* at 0° C. Place the thermometers in finely crushed ice to which has been added enough distilled water to produce a slushy mass. The slush must be thick enough so that both ice and water (without air spaces) extend to the bottom of the vessel. If the lower section of the mass is clear of ice, water of higher density and higher temperature is very likely to lodge in that region and give a false calibration record. Thorough stirring is essential. If the entire mercury column is immersed for 5 minutes or more, the temperature of 0° should be indicated if the thermometer is correctly graduated. Record the facts in the notebook.

185. Correction at 100° C. Assemble the apparatus pictured in Fig. 5, § 33, using a distilling flask of any size from 250 to 500 cc. In place of wire gauze beneath the flask, use a piece of asbestos board in the center of which a hole 3 or 4 cm. in diameter has been cut. Place 100 cc. of pure distilled water in the flask, add two or three boiling stones, and distil the liquid over the Bunsen flame at a moderate rate. When the temperature reading has become constant, record the readings both of the thermometer and of the laboratory barometer. Determine the length of the mercury column which protrudes from the heated zone. Note boiling-point data given in § 446, Appendix, and determine the correction, if any.

If the asbestos board is omitted, heated air creeps up along the upper walls of the flask, and superheats the escaping steam. The resulting temperature record may rise to 101° or 102° and thus be worse than useless.

186. Correction at 218° C. By replacing the water with pure

naphthalene and using the apparatus of Fig. 2 § 23 instead of Fig. 5, the 218° point may be examined, but care must be taken to warm the condenser tube so that the distillate will not solidify and close the condenser passage.

It is somewhat simpler to boil naphthalene in a special Pyrex flask with a neck about 50 cm. long. As illustrated in the accompanying figure, a slender test tube of thin Pyrex glass, holding a small wad of glass wool as a cushion, receives the whole length of the thermometer. With ordinary care, naphthalene may be boiled actively enough to keep the entire mercury column surrounded by the stream of refluxing condensate, and still without appreciable loss of vapors. In about ten minutes the thermometric reading should be constant, and should register the boiling point of naphthalene (218.1° at 760 mm. pressure). For values at other barometric pressures, see the Appendix, § 446.
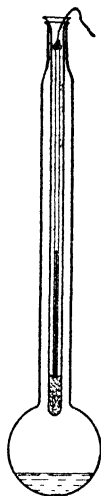
187. Calibration by Melting Point. It is especially convenient in regions of low barometric pressure to calibrate by melting point rather than boiling point. If the standard pure substance is inexpensive, technique similar to that used with ice in § 184 may be employed. Otherwise the standard micro method of determining melting point may be employed, as described in § 203. It may be convenient simply to obtain the apparent melting point of a solid with exactly the same position of thermometer as used with a reference solid. This eliminates stem correction. The following substances, readily obtainable in high purity, may be employed.

p-Dichlorobenzene	53°
Naphthalene	80.1°
Benzil	95°
Benzoic acid	122.4°
Urea	132.7°
Salicylic acid	159.0°

For higher temperatures 3,5-dinitrobenzoic acid (204°), anthracene (216.1°), carbazole (244.8°), and anthraquinone (285°) have been recommended. (Refs. 23, 33.)

EXPERIMENT 3

Separation and Purification

FRACTIONAL DISTILLATION

188. In this experiment a choice is made between two types of apparatus; or part of a class may use each arrangement, with the ultimate aim of testing the efficiency of outfit (*b*).

(*a*) Simple assembly of a 250-cc. distilling flask, water-cooled condenser, and receiver as illustrated in Fig. 3, § 33.

(*b*) A 200-cc. round-bottomed flask fitted with a Hempel, Vigreux, or other suitable fractionating column, as illustrated in § 39, together with condenser and receiver (§ 33).

Provide 120 cc. of one of the mixtures described below. Read § 73 describing the scheme of fractionation into separate receivers, and lay out in the notebook a blank form ready for entry of temperature values, boiling ranges, yields, etc., suited to the case. Probably the exact temperature values cannot be designated in advance, but will require laboratory trial.

Warning. Be careful in fractionating mixtures containing volatile, inflammable liquids lest a receiver containing such material approach too near the flame. Take particular pains to see that an adequate and steady supply of cold water runs through the condenser jacket. One or two boiling stones should be placed in each newly introduced liquid in a boiling flask.

189. Mixtures for Fractionation. Equal volumes (60 cc.) of the following substances are mixed in each case to give the desired material for fractional separation. See inside back cover for data.

(*a*) *Methyl Alcohol and Water.* No azeotropic mixture is possible in this case, and the separation is clear-cut. (See § 79.)

(*b*) *Ethyl Alcohol and Water.* From this experiment one may obtain one of the components (water) in substantially pure condition,

but the other cannot be obtained above the azeotropic composition. (See § 81.)

(c) *Carbon Tetrachloride and Toluene.* A typical example using material of nonpolar or "oil" type. Be sure that the distillation outfit is dry.

(d) *Chloroform and Toluene.* Similar to (c) in general type.

(e) *Benzene and Toluene.* Similar to (c) and (d), but somewhat more difficult.

(f) *Acetone and Water.* Readily separated on account of peculiar boiling point-composition curve. (See § 241.)

PURIFICATION BY RECRYSTALLIZATION

190. In this assignment either a commercial organic product of "technical" grade or an impure laboratory preparation is provided. Look up any available data on solubilities of the compound in question, and read Chap. 9 carefully. Most of the details of procedure are given in that chapter.

Weigh out the designated quantity of the crude raw material, recrystallize, dry the product, weigh it, and calculate the percentage yield for the operation. Compare this yield with the quantity called for by solubility data.

Examples

191. Sulfanilic Acid (commercial grey, crude). Use 10 g. of raw material, and recrystallize from water. About 2 g. of decolorizing carbon (Norite) is required.

192. Acetanilide. Use 5 g. of raw material, and recrystallize from water. See § 161, describing the tendency of this compound to melt and form an "oil" in the solution. Use the method of dilution to eliminate the oil, with the smallest possible quantity of water compatible with satisfactory crystallization. Decolorizing carbon is used if the solution is not colorless.

193. Benzoic Acid (containing both soluble and insoluble impurities). Special mixture prepared for this experiment. Recrystallize a 5-g. sample from water, and use decolorizing carbon.

194. Benzil. In case that this compound is not on the schedule

for later synthetic work, recrystallize 5 g. of the crude or commercial product from ethyl alcohol.   See the last sentence of § 340, and § 341, for further details.   This experiment is suggested here to illustrate supersaturation as well as the use of an organic solvent. Note fire hazard with use of an inflammable solvent (§ 101).

195. *m*-Nitroaniline.   Recrystallize a 3-g. sample from water.

196. Picric Acid.   Recrystallize a 10-g. sample from water. Note that the commercial product presumably contains 10% of water, in conformity with laws governing transportation of material of this type.

SUBLIMATION

197. Hexachloroethane.   A 2-g. sample of this compound is placed in an evaporating dish of about 4 inch size.   A piece of 3-inch filter paper is placed over the substance in the dish, and the whole covered with a watch glass placed convex side up.   The outfit is now placed in a sand bath and heated to a temperature not exceeding 190°, and preferably about 185°, the temperature at which the vapor pressure of hexachloroethane reaches a value near one atmosphere.   It should be noted that too much heating of the sand bath will drive the volatile substance entirely out of the apparatus only too easily, so that close attention should be paid to the temperature.

The vapors of the hexachloroethane gradually work their way upward and finally cause an accumulation of sublimate upon the watch glass.   After the transfer from dish to glass seems to be complete, allow the sand bath to cool to about 120° or less.   Now remove the dish and lift the watch glass over to a paper, or dry open dish, and scrape off the crystalline sublimate.

Since the melting point of hexachloroethane is above the true sublimation point, it is necessary to seal a sample in a completely closed tube for a determination of the melting point.   If you wish to try this experiment, use only a small quantity, and do not heat beyond the melting point.   For the theory of sublimation, with discussion of the behavior of hexachloroethane, see Chap. 14.

198. Anthracene.   About 3 to 4 g. of this hydrocarbon is placed in a 400-cc. beaker which rests upon wire gauze over a stand and

burner. The beaker is covered with a piece of stiff card, or as-
bestos paper, about 15 cm. square, which has a circular opening
about 2 to 3 cm. in diameter cut through the middle. A piece of
filter paper, slightly oversize, is wedged tightly against the per-
forated plate of a 3-inch Buechner funnel. The funnel is inverted
over the beaker and card, and is connected by rubber hose to the
suction service or aspirator. It should be held in position securely
with a clamp.

   Apply gentle suction, thus drawing air from the beaker through
the paper. Heat the anthracene so that vapors, mixed with air,
may pass freely into the funnel, which serves as subliming chamber.
If the heating be too rapid, vapors pass entirely through the paper,
and sublimate gets out into the rubber tube. When little or no
more product seems to be accumulating, allow the apparatus to cool,
collect the anthracene, and wash out the residue of tarry anthracene
with naphtha, benzene, or like solvent mixed with abrasive washing
powder.

EXPERIMENT 4

Determination of Melting Point

PURIFIED⁻COMPOUNDS

199. (*a*) Obtain a sample of the purest benzoic acid available. Since only a very few cubic millimeters of a solid organic compound are required for the determination, a supply roughly equal in volume to a common table pea seed is ample even for repeated trials. Next prepare melting-point tubes and other apparatus for the experiment, as described in § 203, and finally determine the melting point according to § 204 *ff*. Since benzoic acid is a stable compound readily obtainable in highly purified state, this experiment affords a good opportunity to test one's skill in accurate determination at the outset.

(*b*) Using apparatus cited in (*a*), determine the melting points of naphthalene and urea.

(*c*) Weigh out to an accuracy of about 0.01 g. approximately 0.50 g. of benzoic or cinnamic acid, and 0.50 g. of urea. Mix the powdered solids thoroughly and determine the melting point of the mixture. Now prepare as many mixtures of similar total quantity as may be convenient over a range from 10%, 20%, 30%, etc., to 90% of urea. Determine the melting point of each mixture. Two students may cooperate in this project, obtaining eight or more values, which are then to be plotted in the form of a melting point-composition diagram. (See § 153.) Explain the peculiar form of the curve thus drawn.

(*d*) Obtain a sample of a pure organic compound of identity unknown to you, and determine the melting point, using apparatus cited in (*a*).

CRUDE PREPARATION

200. Recrystallization. Obtain a sample of an impure organic preparation of identity unknown to you, and a small specimen of

pure benzoic acid as described in § 208.   The "unknown" material is nominally a single substance, but may be either a commercial product of technical grade or a crude laboratory preparation.   This material is to be recrystallized two or more times, or until its melting point is constant.   Read Chap. 9 on "Isolation of Solid Products" and proceed as follows.

Using very small test tubes (preferably 3/8 to 1/2 inch diameter) test the solubility of the impure solid in common solvents, trying water, alcohol, and benzene first.   First try to dissolve a few crystals in about 0.5 cc. (10 to 15 drops) of the unheated solvent.   If the material is not already finely divided, crush it against the wall of the test tube with a glass rod.   Should the crystals dissolve freely in the cold, the solvent is unsuitable.   Try another solvent.

If the solid does not dissolve freely in the cold solvent, even after crushing, heat the mixture almost to the boiling point.   Should it still fail to dissolve, a new solvent should be tried, presumably one of strikingly different type, as discussed in Chap. 11.   Do not mistake melting of the compound for dissolving.   Mere melting is evidenced by the appearance of oily globules suspended in the hot solvent.

Eventually a solvent should be found which will dissolve the preparation rather freely when hot, and as little as possible when cold.   Do not expect to dissolve minute particles of dust, cork, or other trash which may happen to accompany the preparation and which are obviously not the desired organic compound.   Without attempting to remove impurities, cool the solution in the test tube, if necessary with the aid of an ice bath, to encourage crystallization. The ideal outcome of the experiment is described in § 201 below. If the process does not give such satisfactory result, the trouble may be of the character discussed in § 202.

201. Ideal Conditions.   Under favorable circumstances the solution slowly deposits a moderately small yield of beautiful, distinctly separate crystals, with enough accompanying liquid so that the mixture is easily poured upon a filter.   Such an experiment may then be considered as a model for repetition on a larger scale.   Now decide what vessels, quantity of solvent, fire precautions, etc. are necessary to effect the purification of about half of the sample at hand, and proceed.   See §§ 100 *ff.* for description of apparatus and technique suited to this experiment.

Note that no attempt is made to obtain a maximum or even a

large yield. Frequently the production of a restricted yield of crystals from a relatively dilute solution facilitates filtration and permits the most effective elimination of dissolved impurities. In any case do not use more than 50 cc. of a solvent of appreciable cost, such as alcohol or benzene, with appropriate limitation of amount of substance recrystallized.

If the solution prepared in the test-tube experiment was not clear and transparent, filtration of the main quantity is necessary. If it was tarry, or discolored, decolorizing carbon may be employed. (See § 109.) Pure organic compounds are usually white, often yellowish-white; occasionally of some simple primary color like yellow, orange, or red. Brown, purplish-gray, olive, and other composite pigment tints not recognized in the normal color spectrum generally indicate impurities, and probably a mixture of several or many molecular species.

When the final yield of crystalline material has separated from solution, collect it on a filter and wash it cautiously with a few cubic centimeters of cold solvent of the kind you have been using. Now set aside a small sample (5 to 10 mg., estimated) to dry between filter papers and eventually to serve for the first test of melting point. Immediately recrystallize the remainder from fresh solvent, again preserving a small sample. This operation may be repeated two or three times, or until there seems to be no further improvement in appearance of the crystalline material.

Sometimes a compound will crystallize with solvent of crystallization, leading to a false determination of melting point with respect to the pure substance. Such an error is neatly obviated by changing solvents during the successive crystallization operations just described. In any event, the final array of successively recrystallized samples is tested in the melting-point experiment to follow. If the last two recrystallizations give products which not only melt sharply, but also agree exactly in melting point, there is assurance that you have really purified the preparation, and thus may make a critical comparison with melting-point data given in the literature.

202. Difficulties. If the program of § 201 (above) does not go forward smoothly, one of the following options may fit your situation.

(*a*) The small test-tube sample of solution, upon cooling, may suddenly "set" to an apparently solid crystalline cake which would seem to be un-

workable on a filter. Actually this mass may not contain much solid matter.
If stirred with a glass rod, the material may prove sufficiently fluid to permit
filtration.   If still too solid, carefully add more solvent, drop by drop,
frequently reheating and cooling, until the solution is so dilute that some
time is required—perhaps 5 minutes or more—to obtain loosely crystalline
material upon cooling. Now proceed with the experiment on a larger scale,
as already described in § 201.

(b) The sample of solution upon cooling becomes turbid. Droplets of a
so-called "oil" separate, run together, and either sink or float according to
density.   In such a case it is possible that a change of solvent is needed.
Either the experiment should be repeated with a new solvent, or the new
solvent should be cautiously added to the mixture of the old solvent and solid
already prepared. If the oil has appeared in an aqueous solution, the addi-
tion or substitution of ethyl alcohol may eliminate the oil and permit a neat,
direct crystallization of solid.   If the trouble has occurred in alcohol or
benzene solution, a shift of similar kind to light petroleum (light ligroin) may
solve the difficulty. Be careful, however, not to bring together two solvents
that are not miscible with each other, such as water and benzene.

With aqueous solutions, where cost of solvent is of no concern, a simpler
remedy for the oil difficulty is found in mere dilution. The hot solution of
the compound is cautiously diluted until it no longer is capable of depositing
a second phase in the temperature zone where the oil occurs. Care is taken,
nevertheless, to have the solution still sufficiently concentrated so that when
it is finally chilled in the ice bath an adequate yield of crystals will be pre-
cipitated. (See § 161.)

The above method of simple dilution to avoid the "oil" difficulty is pre-
sented merely as a device to serve this experiment, where high yield is not
essential.   In synthetic procedures the plan would be considered wasteful in
view of the excessive residue left in the mother liquor. Evaporation of such
a mother liquor, for the purpose of salvage of the residual material, is usually
unsatisfactory.

(c) If no crystals are obtainable even from extremely concentrated solu-
tions cooled in an ice bath, try "seeding" the solution with a minute crystal
of the original preparation. Try also to stimulate initial crystal formation
by scratching the side wall of the crystallizing vessel with the end of a glass
rod. If these tricks are not successful, try a change of solvents or a mixture of
solvents. For example, should ethyl alcohol be too effective a solvent, try
adding water drop by drop. Sometimes compounds containing hydroxyl
groups crystallize in very sluggish fashion from water or alcohol, but come
out more rapidly from benzene; in some cases most rapidly and neatly from
light ligroin. If benzene is too effective, one may try diluting it with a sol-
vent more highly oxidized (alcohol) or with one more reduced (ligroin).

DETERMINATION OF MELTING POINT

203. Preparation of the Tube.   Thin-walled glass tubing is required as material from which the tubes are made.   Pyrex glass is preferable, but requires a blast lamp with compressed oxygen
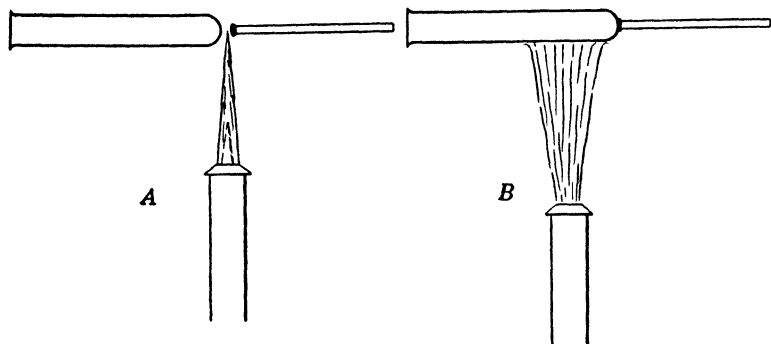
service.   Ordinarily a 12-mm., or half-inch, soft-glass test tube is the best form in which suitable glass may be procured from an ordinary commercial supply or storeroom.

Using a small blast flame, heat the closed end of the test tube with continuous rotation, as shown at *A* in the illustration.   Simultaneously heat the end of a piece of glass rod or tubing in like manner. When the tips of both pieces of glass are bright red hot and plastic, firmly seal them together with as little crumpling or twisting of the plastic joint as possible.   Now hold the joined tube in a straight line until the seal is just rigid enough so that no bending will take place.

At once shift the test tube with its convenient handle to position *B*, where it is now to be strongly heated, with continuous rotation, at the *tip* of a large brush flame.   A little practice enables the beginner to rotate the tube without twisting the softened portion, until a stretch of 3 to 5 cm. of the tube is very soft but has not yet collapsed.

At this point remove the tube from the flame, and immediately draw it out until the external diameter has shrunk to a range of 1 to 2 mm.   Now pause for 2 or 3 seconds with hands in the outstretched position to ensure solidification of the slender tube before it can bend.

If the student uses artificial gas, which gives a hotter flame than natural gas, and has a Bunsen burner and wing-top attachment in good order, he may conduct the above operation fairly well with these devices instead of the blast lamp. The blast lamp is much better, however, for quick production of a good supply of melting-point tubes.

The slender melting-point tube may now be cut into 15 cm. lengths. For this operation the sharp edge of a freshly fractured piece of porous clay plate is much more satisfactory than steel tools, which crush the fragile tubing. Both ends of each 15-cm. length are quickly sealed by just barely exposing the tips to a hot gas flame. In this manner each length will be sealed airtight from the start, and may be preserved indefinitely free from dust and moisture on its inner surface. When a melting-point tube is needed, cut one of these double-sealed tubes in half, thus obtaining two tubes of convenient length.

204. Introduction of Material. Insert the open end of the .melting-point tube into the mass of powdered crystalline solid, thereby introducing enough material to occupy 3 to 5 mm. of the length of the tube. After an adequate quantity has been caught in the mouth of the tube, tap the tube, closed end down, on a wooden table, until the particles finally reach the bottom.

205. Manipulation. The tube with its enclosed sample of crystalline material is now to be placed beside a thermometer (0° to 360° range) so that the organic compound lies close to the mercury well. If sulfuric acid is used as the bath liquid, experienced workers take advantage of its surface tension, and merely lay the tube along the thermometer which has been wetted with the acid in advance. No fastening device is used. Such workers consider the rubber band shown in the accompanying figure as a sort of crutch indicating weak technique; ask your instructor! The slender rubber band is cut with scissors from the end of a piece of fresh, soft, 3/16-inch rubber tubing. Care is taken to keep it well out of the bath.

Now assemble apparatus suitable for the heating of the tube, with use of an approved bath liquid, according to the directions given by the instructor. Three commonly used arrangements are shown in the accompanying figure; see § 147 for discussion of relative merits of bath liquids.

206. Use of Beaker. With the aid of a Bunsen or blast flame bend a piece of 4 or 5 mm. glass rod into the form of a loop with handle as shown. Use this bent rod as a stirrer, which may be raised and lowered without interference with the thermometer or melting-point tube, thus ensuring uniform temperature.

207. Use of Flask. Use a Pyrex flask of 50 to 200 cc. capacity. If the convenient long-necked round-bottomed flask shown above is
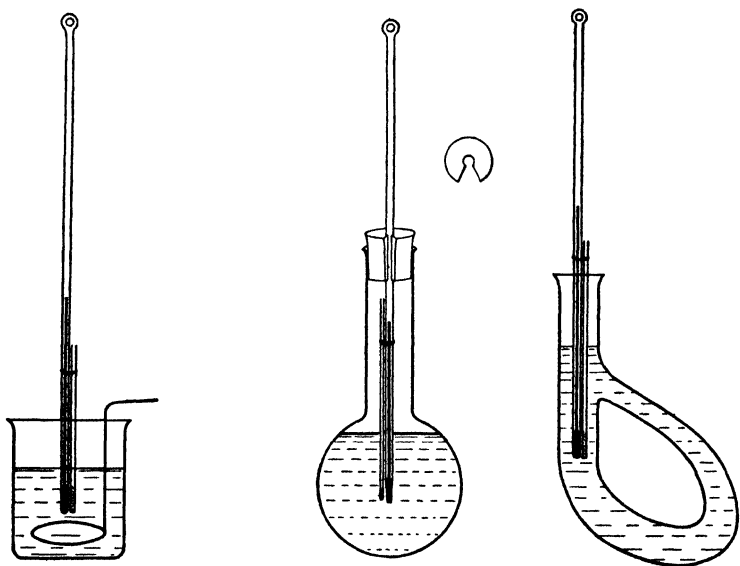
Apparatus for Determination of Melting Point

not available, use a 125-cc. distilling flask, allowing the side stem, unnecessary here, to hang behind and out of the way. Do not fill the flask to a level higher than that shown in the diagram, lest the bath liquid eventually overflow because of expansion at high temperatures. No wire gauze is used. Heat the flask at the bottom only with a very small flame. Such an outfit is particularly favored where there are determinations made from day to day, and thus where it would be undesirable to expose a bath liquid in an open vessel continuously. Although the stirring device featured with the beaker

assembly is missing, it is surprising how accurately a melting point may be determined with the flask arrangement.

The third, or modified Thiele apparatus, facilitates circulation of the bath liquid, at the same time preserving the convenience of the flask method.

208. Practice in Determination. Provide two or more melting-point tubes containing pure benzoic acid, and place one in proper position for the determination. Heat the vessel steadily at first until the temperature is within 6° to 8° of the probable melting point— that is, to about 115° in the case of benzoic acid. Now heat slowly— at a rate between 1° and 2° per minute. The acid should melt sharply at 122.4° (corr.). Repeat the determination, each time with a new melting-point tube, until you can reproduce with confidence this known value. It will of course be necessary to correct the direct reading for emergent stem, and possibly for error in the graduation of the thermometer. (See § 19.)

209. Melting Point of "Unknown" Substance. Heat a melt-ing-point tube containing a sample of your purified unknown sub-stance rapidly in order to determine approximately the melting temperature. Discarding this first tube, make a final accurate determination on a new tube, noting whether the product melts sharply or over a range. Record in the notebook the temperature when melting started and that when the last crystal disappeared. If this melting range is more than one degree, an excessive amount of impurity is suspected, and the process of purification of the material should be continued.

210. Sources of Error. Too rapid heating may easily lead to a false record of melting range even with a pure substance. The whole mass of the organic compound may not have time to melt be-fore the temperature of bath and thermometer rises above the true melting point. Furthermore, many inexperienced workers report single melting-point values which are too high, again because of too rapid heating. In such cases the finely divided organic compound, filled with air spaces, conducts the heat poorly, and does not arrive at the true melting temperature as fast as the highly conductive mercury of the thermometer. If the melting-point tubes have ex-cessively thick wall this trouble is still further aggravated. See Chap. 12 for theory of this determination.

EXPERIMENT 5

Molecular Formula

MOLECULAR WEIGHT FROM MELTING POINT

211. The determination of the molecular formula of an organic compound normally calls for two quantitative experiments, namely:

(*a*) Elementary analysis, leading to the simplest formula. For example, octane yields the simplest formula C_4H_9.

(*b*) Determination of molecular weight, which shows whether it is necessary to multiply the coefficients determined in (*a*). In the example of octane, the factor of two is required, yielding the final formula C_8H_{18}.

Obtain a sample of an "unknown" organic compound, together with the figures for weight of carbon dioxide and water found in the quantitative combustion analysis of a specified weight of the compound. (The actual determination of such figures requires special apparatus and experience not called for in this course.)

Using a quantitative balance, weigh out to the accuracy of 1 mg. not less than 0.190 or more than 0.210 g. of the unknown compound into a dry test tube, and record the weight in the notebook. Add to this a sample of pure camphor, weighed to like accuracy, ranging from 1.95 to 2.05 g. Heat the mixture gently over the Bunsen flame until it has entirely melted, and see that all parts of the materials are thoroughly mixed. Take care that neither camphor nor other volatile substance sublimes in part in the upper part of the tube. Stir the mixture with a glass rod and immediately cool until the material is solid. Place 1 mg. or more of the mixture in a melting-point tube and determine the melting point as described in § 205. Record the temperature at which the last crystals disappear as the melting point of the mixture. Determine also the melting point of unmixed camphor taken from the same lot as the original sample. Since only the *lowering* in melting point is important in this experiment, neither a very small impurity in the camphor nor a calibration error of the thermometer is of great significance.

Calculate the simplest formula of the compound from the combustion

data furnished by the instructor.   Next calculate the molecular weight,
using the value 39.7 as the cryoscopic constant for camphor.   Such a calcu-
lation is based upon the following statement, which is approximately true
provided mixtures of nearly 1 to 10 ratio are considered.   One mole of a
solute normally lowers the melting point of 1000 g. of camphor by 39.7° C.
Incidentally, compounds of a type where the lowering is abnormal will not
be issued in this experiment unless notice to the contrary is given.   Further
information is given in *J. Biol. Chem.* **75,** 289(1927).   Finally, from the sim-
plest formula and the determination of molecular weight, calculate the
molecular formula of the compound.

Combustion analysis is conducted by either of the following standard
methods, which differ fundamentally only in size of the samples weighed.
Especially good descriptions of these methods are given by the authors cited
below:

Macro (large scale) method: Fisher (Ref. 33).

Semimicro (intermediate) method: Fieser (Ref. 31).

Micro (small scale) method: Pregl-Roth-Daw, *Quantitative Organic
   Microanalysis,* Blakiston's, Philadelphia, 1936, and Niederl and Niederl,
   Micromethods of Quantitative Organic Elementary Analysis, 1942, Wiley,
   New York.

EXPERIMENT 6

Absolute Alcohol

212. Many laboratory and industrial processes require the use of nearly pure ethyl alcohol, in which the content of water is much below 1%, and preferably not over 0.2%. Such alcohol mixes with certain oils freely, whereas 95% alcohol does not. Unfortunately this dry, or "absolute," alcohol is not readily prepared by ordinary fractional distillation. One solution of the problem is obtained by mixing quicklime (calcium oxide) with commercial aqueous ethyl alcohol. The quicklime combines with the water to form calcium hydroxide, leaving the alcohol behind practically free from water.

213. Calculate the quantity of quicklime which is required by theory to react with the water present in 150 cc. of commercial ethyl alcohol. The commercial product supplied to the author's laboratory as this is written contains approximately 92% by weight of ethyl alcohol, the balance being almost all water. (It is commonly called "95% alcohol," the figure being a rough approximation of the percentage by volume, as customary in distillery practice.) Use the *weight-per cent value only*, as calculations "by volume" involve unnecessary arithmetical labor. If the laboratory alcohol differs from the standard above mentioned, the instructor will give notice of the deviation.

As technical quicklime is not pure, weigh out on a rough balance double the amount calculated above. Select only hard pieces varying from about 4 to 15 mm. in diameter, rejecting all powdered material, much of which may already be slaked.

Place the alcohol and quicklime in a 700 or 1000 cc. Florence flask or a round-bottomed flask and warm the mixture by placing the flask in a pan of hot water for a few moments. As soon as the temperature of the alcohol has reached 60°, stopper the flask tightly and set it away for 2 to 7 days. Read § 24 before resuming operations.

After the proper time interval attach a water-cooled reflux condenser to the flask and place the flask in a water bath. A calcium chloride tube may be mounted on the top of the reflux condenser.

If the experiment is being conducted in very dry summer or fall weather, with the relative humidity below 30%, the calcium chloride tube is of little use, and may be omitted. In such case a piece of cotton is used instead, to hinder atmospheric diffusion.

Heat the water bath until the alcohol in the flask boils quietly, and continue the refluxing process for an hour or more. Now rearrange the outfit for ordinary distillation, using a setup similar to that pictured in Fig. 1, § 33. The thermometer may be omitted. On the extremely dry days above cited a simple flask may be substituted for the suction flask and calcium chloride tube; but in such a case be sure that there is no stopper connecting the receiver with the condenser. Even in dry weather the filter flask and calcium chloride tube are used if one desires a preparation over 99.8% pure. In rainy weather their omission may reduce the purity of the final product even below 99%. Yield 115 cc. including test samples.

If the laboratory is provided with the special paraffin oil for water test, proceed as described in § 214 below. If such oil is not available, dicyclohexyl (§ 216) may be used. If no suitable test oil is available, follow directions of § 217.

214. Distillation; with Estimation of Water Content. Distil the alcohol, collecting the first 4 or 5 cc. of product in a small dry test tube, which is immediately corked and set aside. Collect the next 4 or 5 cc. in a second test tube, and preserve in like manner. Now connect the condenser to its regular receiver and proceed with the main distillation. While this distillation takes place, determine the percentage of water in each of the two samples of alcohol already collected, using the quantitative paraffin-oil method described in § 215 below.

As the distillation nears completion, collect another sample in a test tube, and determine its water content. When the alcohol has all come over, shake the receiver containing the principal yield of absolute alcohol, to ensure uniform mixing. Now withdraw a 3-cc. sample of this main product and determine its water content. Report this as the test on your preparation as submitted to the instructor or assistant.

Caution. In cleaning out the flask, empty the residue of slaked lime into the waste jar, not the sink!

215. Procedure of Test. Measure just 3 cc. of the alcohol to be tested from a dry graduate into a dry 6-inch test tube. Add just 3.2 cc. of "Standard Paraffin Oil Mixture" (page 363) and stir with a dry thermometer.

Heat the liquid until it becomes clear—that is, until it goes into one phase. Alternately cool and heat the tube, with constant stirring, until you are able

to determine to a nicety the temperature at which the clear liquid just begins to show turbidity. Consult a graph or table which shows directly the corresponding percentage of alcohol. The accompanying graph applies to the particular oil used in the author's laboratory at the time these directions were written.

If the process of dehydration has been conducted carefully, the percentage of alcohol will be above 99, and often exceeds 99.6. See § 144 for a discussion of the theory of this test.
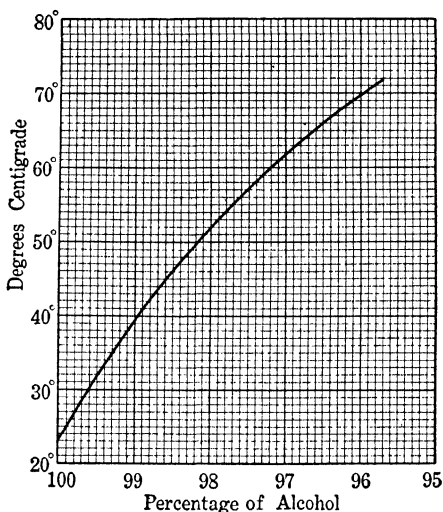
Miscibility Temperatures of Oil with Ethyl Alcohol Containing Small Amounts of Water

This graph shows the maximum temperature at which a mixture of 3.2 volumes of "Standard Paraffin Oil No. 4A" and 3 volumes of aqueous or absolute alcohol exists in two phases, that is, is turbid when stirred. It is assumed that no other impurity than water is present in the alcohol.

216. Use of Dicyclohexyl. If only a few determinations are required, the hydrocarbon dicyclohexyl is an acceptable though more costly substitute for the paraffin oil. Use 4 cc. of dicyclohexyl with 2 cc. of the alcohol, and determine the temperature at which the opalescent (not clear) solution suddenly becomes turbid, so that the immersed section of the mercury thread of the thermometer is no longer discernible.

Alcohol	100%	99.9ꞌ	99.8	99.7	99.6	99.5	99.0	98.5
Temp.	23.4°	25.4°	27.3°	29.2°	31.0°	32.8°	41°	48°

217. Distillation; with Qualitative Test. If the special paraffin oil called for in § 215 is not available, simply distil the whole quantity of alcohol in two fractions. Collect the first 4 or 5 cc. in a small dry test tube, and the balance in the regular receiver normally provided. Divide the first sample of distillate into two approximately equal parts. To one add a few particles of anhydrous copper sulfate, and to the other a crystal or two of potassium permanganate. Test in a similar manner very small samples of the main alcohol distillate. The appearance of a coloration in any case indicates the presence of more or less water. On the other hand, these salts are practically insoluble in really absolute alcohol. These tests are admittedly inferior, and not comparable with the oil method of § 215 above.

Determine the theoretical, actual, and percentage yields (including the quantities set aside for test). Note the density data given below.

218. Density of Alcohol at Various Temperatures.

Percentage	DENSITY		
by Weight	*15°*	*20°*	*25° C.*
90%	.822	.818	.813
91	.820	.815	.811
92	.817	.813	.808
93	.814	.810	.805
94	.811	.807	.803
95	.809	.804	.800
96	.806	.801	.797
97	.803	.798	.794
98	.800	.795	.791
99	.797	.792	.788
100	.794	.789	.785

Optional Experiments

219. Other Alcohols. Methyl alcohol may be dehydrated in a manner similar to that given above. On account of its lower boiling point, methyl alcohol should be handled with greater precaution against fire. (See § 34 (*b*).) In this case *n*-hexane is substituted for the special paraffin oil [*J. Am. Chem. Soc.* **48,** 1929 (1926)]

Alcohols with more than two carbon atoms per molecule are more easily dehydrated. When one of these is shaken with solid potassium hydroxide,

two liquid phases are formed, the lower of which contains the larger part of both the water and caustic alkali, and which is discarded before distillation of the alcohol.

For preparation of extremely dry alcohol, see § 361.

Questions

1. What is the chemistry of the action of the calcium oxide?

2. Why is a water bath used here?

3. Is there any objection to the use of another drying agent? For example, calcium chloride, sulfuric acid, phosphorus pentoxide, sodium sulfate.

4. Is there any objection, aside from expense, to the use of sodium metal as a dehydrating agent?

5. Why is the process of fractional distillation not adequate to rid the alcohol of water?

6. Why do the earlier fractions of the distillate have a different water content from that distilled later? Explain with the use of a boiling-point diagram.

EXPERIMENT 7

Ethyl Iodide

$$3C_2H_5OH + PI_3 \rightarrow 3C_2H_5I + P(OH)_3$$
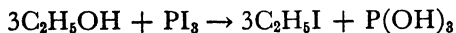
220. Phosphorus iodide, called for in the typical equation given above, is not commonly available commercially. A reacting mixture of the less expensive free elemental substances, phosphorus and iodine, is used. Red phosphorus is preferred to the extremely active yellow form both for safety and convenience in control of the reaction.

To a 200-cc. round-bottomed flask fit a water-cooled reflux condenser as described in § 24. Now set the condenser aside temporarily, and place 30 cc. of ethyl alcohol and 2.5 g. of red phosphorus in the flask. Absolute alcohol is preferable, but 95% alcohol will give good results. Add gradually, in small portions, 25 g. of iodine crystals. Shake the mixture frequently during the addition, and cool it from time to time by immersing the body of the flask in cold water. This tends to prevent loss of the volatile product by evaporation. As soon as there seems to be no further evolution of heat, stopper the flask tightly with a well-fitted cork and set it aside for a day or more. (If laboratory arrangements permit, the flask may be set aside under reflux condenser instead of a simple stopper, and the upper end of the condenser loosely plugged with cotton which is removed just before the next operation.)

At the next laboratory hour place the flask, with attached reflux condenser, in a steam or water bath, and boil the iodide mixture very gently for 1 hour. Now rearrange the apparatus for ordinary distillation, using wire gauze. Use a small flask as receiver, and place it in an ice-water bath. If a thermometer is included (optional) it will be convenient later to tell when the crude ethyl iodide is completely distilled.

Using a small, quiet blue flame, distil the reaction mixture until the temperature reaches about 95°, and collect the crude, colored product in a receiver cooled in an ice-water bath. A slight additional yield of distillate is obtainable if the flame is played gently over the unprotected bulb for a few seconds, but do not heat strongly, lest a quantity of dark-colored decomposition products go over and contaminate the product excessively.

With the aid of a common iron ring, mount a small separatory funnel on a stand, and see that any paper strips are removed from ground glass stoppers and stopcock plug. Treat the latter with a small quantity of stopcock lubricant. In this funnel place the crude ethyl iodide, and add about 20 to 30 cc. of approximately 1N sodium hydroxide solution. Stopper the funnel, shake thoroughly, and then allow the two liquids to separate. Run out the ethyl iodide layer into a small flask, taking care not to let the aqueous wash liquid follow. (If the iodide does not run out freely, close the stopcock; what is wrong in your adjustment of the apparatus?) Now pour out the sodium hydroxide layer from the top of the funnel. Repeat the washing process, using water alone this time. (See further explanation of washing in § 87.)

Transfer the colorless product, free as possible from excess of water, to a small conical flask, and add about 1 g. of granular calcium chloride. Stopper the flask tightly and allow the preparation to stand over night.

Place a piece of glass wool or cotton about the size of a pea in a small funnel, and filter the dried ethyl iodide through this into a dry distilling flask of from 50 to 125 cc. capacity.

Mount the flask over a water bath, and distil through a water-cooled condenser into a small flask which rests in an ice-water bath. Preserve the distillate in a tightly stoppered bottle. Yield, 20 g. Boiling point of ethyl iodide, 72°. Upon standing, the substance soon turns pink, then amber or brown, owing to separation of iodine. A minute globule of mercury kept in the preparation absorbs this iodine and prevents the discoloration.

Note. If the fingers should become stained with iodine, wash with sodium thiosulfate solution, which is kept on the laboratory shelf for such purpose. Failure to follow this advice promptly may result in serious irritation of the skin.

Optional Experiment

221. Methyl Iodide; an extremely volatile liquid (Refs. 13, 25, 26, 27, 30, 35, 39, 45).

Questions

1. Why should absolute alcohol be preferred in this experiment? What inorganic side reaction might be promoted if 95% alcohol were used?

2. Why is the side reaction not considered to be of serious importance?

3. Explain how ether might appear as a by-product in this experiment.

4. Suppose you substituted the very active yellow phosphorus for red phosphorus in order to profit by the greater speed of reaction possible with the former. How would you change the technique and the apparatus so as to keep the reaction under control? [See *J. Am. Chem. Soc.* **41,** 789 (1919).]

5. What chemistry is involved in the use of sodium hydroxide to remove free iodine from the crude product?

6. What is the nature of the reaction of iodine with the sodium thiosulfate used to wash stained fingers in this experiment?

7. How do you decide whether phosphorus, iodine, or alcohol is the factor upon which to base your calculation of theoretical yield? (See § 29.)

EXPERIMENT 8

n-Butyl Bromide

$$C_4H_9OH + KBr + H_2SO_4 \rightarrow C_4H_9Br + KHSO_4 + H_2O$$
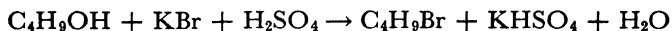
222. When a primary alcohol is heated with hydrogen bromide, the corresponding normal alkyl bromide is produced. Concentrated aqueous hydrobromic acid is a suitable but relatively expensive reagent for the purpose. A mixture of potassium or sodium bromide and sulfuric acid serves as an economical substitute, which gives good results provided the acid is used at fairly high concentration. If sodium bromide is used, it is thus important to allow for possible water of crystallization when the appropriate quantity of ordinary water is to be provided.

Add 0.6 mole of potassium bromide or anhydrous sodium bromide to 0.5 mole of *n*-butyl alcohol contained in a 500-cc. round-bottomed flask. Attach a water-cooled reflux condenser as shown in § 24, using a simple wire gauze in place of a water bath for support. Prepare a sulfuric acid solution as follows: To 40 cc. of cold water in a 250-cc. flask add 70 cc. of concentrated sulfuric acid in a fine stream, keeping the contents of the flask well mixed by an occasional swirling motion of the vessel. When all of the acid has been added to the water, cool the resulting solution by running cold water over the body of the flask. Now add from half to two thirds of this acid solution to the butyl alcohol-bromide mixture by pouring it through the reflux condenser, using a funnel to prevent spilling. Loosen the clamps holding flask and condenser and shake the flask until its contents are well mixed. Now replace the clamps and start water flowing through the condenser jacket. If the experiment is not conducted in a hood, connect the upper end of the condenser by means of a short tube to an inverted funnel whose mouth is placed near but not actually in a quantity of water in a large bottle or beaker like that shown in the figure of § 251.

Using a small Bunsen flame, heat the solution to boiling, and

adjust the rate of heating so that the liquid drips back slowly from the end of the condenser. After this reflux operation has continued for 30 to 40 minutes, slowly add the rest of the sulfuric acid solution through the condenser. Now continue heating until the total period of refluxing has reached 2 hours. The experiment may now be interrupted if time is limited; but upon resumption of work the process should be carried out without further interruption until the product is set aside for a day to dry over calcium chloride or magnesium sulfate.

The apparatus is now rearranged for ordinary distillation. (See illustrations in § 33.) A thermometer is included, and the mixture is distilled through a water-cooled condenser from the flask over wire gauze. Note the peculiar behavior of the thermometer and compare its reading with the boiling points of the components of the reaction mixture. (See discussion in § 83.) Distillation is now carried out until only a water-soluble phase seems to be coming over; that is, no further globules of "oil" are apparent in the condenser. This result is attained usually by the time the temperature has reached 110°.

With the aid of a common iron ring mount a separatory funnel on a ringstand. After seeing that any paper slips are removed from ground glass parts, treat the dry stopcock with a small amount of stopcock lubricant. With the aid of the funnel, separate the crude reaction product, or oil, from the watery portion of the distillate. Which is the butyl bromide layer, upper or lower? Wash the crude butyl bromide with 25 cc. of cold concentrated sulfuric acid (preferably chilled in an ice bath to reduce fume nuisance). Run off the sulfuric acid, decant the butyl bromide into a small flask, and wash the funnel and stem with faucet water. Replace the butyl bromide in the funnel, wash with about 25 cc. of N sodium hydroxide, and finally with water. (See § 87 for discussion of technique in washing.)

With careful separation of liquids, run the bromide layer into a small dry conical flask. Add about 3 g. of granular anhydrous calcium chloride or magnesium sulfate, and allow to stand for a day or more. If it is necessary to complete the experiment more promptly, shake the mixture of drying agent and butyl bromide until the liquid seems to be clear and free from emulsified water. Finally filter through a loose wad of glass wool about the size of a pea, allowing the liquid to pass into a small distilling flask held in

such a position that liquid cannot reach the sidestem. Retain the drying flask with residual drying agent until it is certain from the next process that it is no longer needed.

Mount the distilling flask upon a wire gauze, attach a water-cooled condenser, and distil. If the first part of the distillate is turbid, the drying process was not complete; return all of the liquid to the drying flask.

The liquid boiling between 99° and 103° is substantially *n*-butyl bromide. Yield, 55 g. Boiling point of pure *n*-butyl bromide, 101.6°.

n-Propyl, *n*-amyl, iso-amyl, and higher bromides may be prepared in high yields by the same method as given above for *n*-butyl bromide, but require two to four times the period of refluxing. These longer periods give only a slightly improved yield in the case of the *n*-butyl derivative.

Optional Syntheses

223. Methyl Bromide, b. pt. 4.6°. Illustrating preparation of an extremely volatile liquid, condensable in ice-salt mixture, and preserved in a stout-walled sealed tube, which should be tested after completion under safety precautions; consult the instructor. Methyl bromide may also be used directly as a gas in standard synthetic procedures (Ref. 44).

Ethyl Bromide, b. pt. 38°. Readily obtained by the rapid reaction of ethyl alcohol with the bromide-sulfuric acid mixture (Refs. 1, 16, 26, 27, 30, 34, 35, 38, 39, 40, 41, 43, 45).

Questions

1. What is the purpose of the sulfuric acid in this experiment?

2. What difference in method would you think advisable if ethyl bromide were to be made instead of the butyl derivative? If methyl bromide were required?

3. How could you reverse the main reaction of this experiment; that is, recover *n*-butyl alcohol from the bromide? Devise apparatus for accomplishing this, keeping in mind the physical and chemical properties of the substances involved.

4. What is the purpose of the sulfuric acid used as a washing liquid? Of the sodium hydroxide?

5. Why is the boiling point of the mixture of crude butyl bromide and aqueous residue below 100°, although water (b. pt. 100°) is the lowest boiling ingredient in the mixture?

EXPERIMENT 9

tert-Butyl Chloride

$$(CH_3)_3COH + HCl \rightarrow (CH_3)_3CCl + H_2O$$
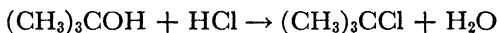
224. Replacement of the hydroxyl group is much easier to accomplish in a tertiary aliphatic alcohol than in primary or secondary alcohols. No zinc or phosphorus halides, and not even boiling temperature, are required. The halogen acid must, however, be of high concentration.

In a 200- or 250-cc. separatory funnel place 0.3 mole of *tert*-butyl alcohol. The anhydrous alcohol is best, but constant-boiling (88%) alcohol will do fairly well. To this add 80 cc. of concentrated hydrochloric acid (sp.g. 1.19), and at intervals shake the mixture well. Usually hydrochloric acid of such high concentration is available only in the C.P. grade. After 20 minutes discard the aqueous layer, and wash the remaining layer of crude *tert*-butyl chloride with a 5% solution of sodium bicarbonate. After all acid seems to have been eliminated, wash the product with water until it is neutral to moist litmus paper. Dry the preparation over calcium chloride or magnesium sulfate (about 5 g.) and distil through an effective water-cooled condenser into a receiver cooled with ice. Collect the fraction boiling at 49° to 52° and preserve in a bottle containing two or three small pieces of anhydrous calcium chloride. Yield, 20 g. Boiling point of pure *tert*-butyl chloride, 51°.

Questions

1. What change in technique would be necessary if the *tert*-butyl alcohol were replaced with

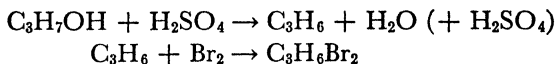   (*a*) *sec*-butyl alcohol?   (*c*) methyl alcohol?
        (*b*) *n*-butyl alcohol?

2. Which of three isomeric butyl chlorides would be most easily preserved pure in a moist atmosphere, the primary, secondary, or tertiary?

EXPERIMENT 10

Propylene and Propylene Dibromide

$$C_3H_7OH + H_2SO_4 \rightarrow C_3H_6 + H_2O \; (+ H_2SO_4)$$
$$C_3H_6 + Br_2 \rightarrow C_3H_6Br_2$$

225. When an aliphatic alcohol is heated with sulfuric acid of suitable concentration, hydrogen and hydroxyl are removed from the molecule, leaving an unsaturated hydrocarbon, or alkene, as a residue. In some cases an alkyl-sulfuric acid, of general formula $R-OSO_3H$, is produced as an intermediate product; in other cases a different mechanism of reaction is presumed to exist. The process above outlined is carried out with some difficulty in the case of primary alcohols (§ 227), more easily with secondary (§ 225), and with greatest ease in the case of tertiary (§ 229).

A secondary alcohol, such as the isopropyl derivative chosen here, reacts even with slightly diluted sulfuric acid, and the oxidizing tendency of the concentrated acid, which is involved in the procedure of § 227, is thus minimized. The resulting propylene gas is passed through ice and salt, so that any alcohol vapors will be condensed and prevented from reaching the bromine tube where an offensive by-product would otherwise be produced. Bromine finally adds directly to the purified alkene. Although readily performed by a careful though inexperienced student, this experiment is somewhat more difficult than the time-honored ethylene dibromide synthesis, and thus is more distinctly a test of skill as well as a novelty.

Arrange the apparatus represented in the illustration, using a 1-l. distilling flask, a 500- or 1000-cc. filter flask, and an 8-inch test tube in the beaker. The filter flask carries a small open safety tube about 60 cm. long. Rubber stoppers are preferable to corks for the two flasks, since the gaseous product passes to the bromine tube under some pressure. Corks of excellent quality, very carefully rolled and bored, may be used, however. The inlet tube of the test tube must reach almost to the bottom of that vessel. If this precaution is not observed, difficulty will be experienced in getting the dense liquid bromine to diffuse up into the zone of the absorption reaction. A small supply of ice is kept at hand so that the water

surrounding the test tube may be kept at the vicinity of 10° to 15°. If the bromine is too cold, it will not react readily, and may solidify. Much propylene is then lost. If too warm, bromine evaporates
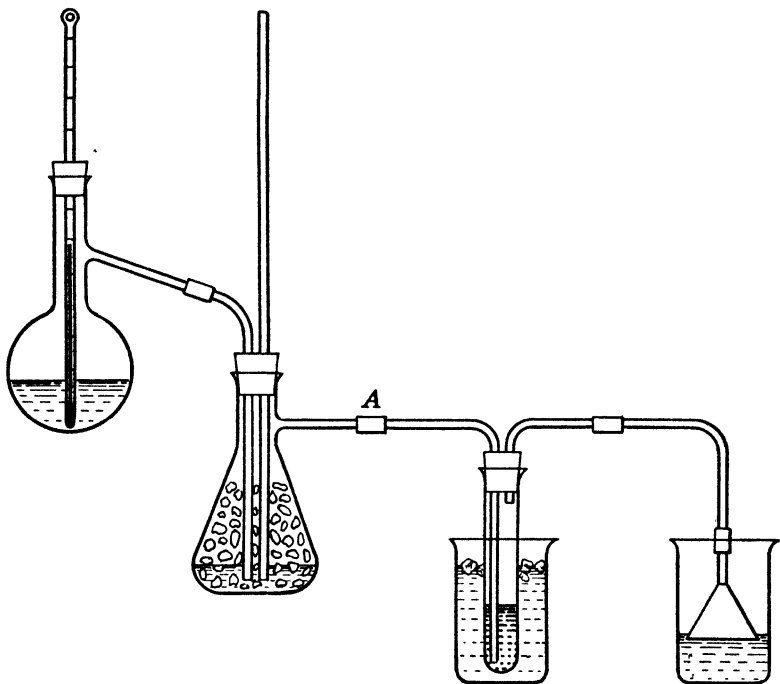
excessively, causing loss of yield and offensive fumes in the laboratory.

The small amount of noxious vapors which escape from the last test tube is caught in a beaker. The funnel should *just touch* the surface of the liquid in the containing vessel. Under such circumstances it will be impossible for the liquid to be sucked back into the bromine tube in case of reversal of pressure. The addition of ice to the beaker at the right helps in controlling bromine fumes.

Carefully pour 50 cc. of conc. sulfuric acid into 25 cc. of water in a flask, and mix well. Cool the resulting solution and add it slowly, with thorough mixing, to 75 cc. of isopropyl alcohol together with a few boiling stones contained in the distilling flask of the illustration. Now fill the filter flask as full as possible of a mixture of crushed ice

and salt (approx. 5 to 1). Test the assembled apparatus with air or gas to see that there are no leaks.

Go outdoors, or to a hood, place just 10 cc. of bromine in the test tube, and complete connection of apparatus. (**Warning.** Bromine is a dangerous reagent, attacking the skin vigorously. If even the slightest amount is spilled upon the skin, wash at once under the faucet, and treat the wound promptly with sodium thiosulfate; see information on the inside front cover. *Do not take bromine from stock for this experiment until you are prepared to go ahead with the work.* If bromine is left in the student's locker, there will be evaporation, corrosion of equipment, and an odor nuisance in the laboratory. If the bromine is chilled in ice, or taken just when needed from the refrigerator, it is handled with less discomfort.)

Temporarily disconnect the rubber tube at point A of the illustration. Now heat the generator flask until a lively current of propylene gas is running, and until most of the air in the flasks has been expelled. This diversion of the air minimizes the nuisance of blowing bromine vapors entirely through the apparatus before start of reaction. Now reconnect the tube at A and pass propylene through the bromine until the latter is decolored. Avoid excessive heating of the flask, lest an undue amount of alcohol be merely distilled into the ice mixture. Such distillation causes rapid melting of the ice, loss of ultimate yield, and is likely to cause formation of noxious byproducts.

After sufficient propylene has passed to decolor the bromine, or to reduce the color to pale yellow, stop the generation of gas and transfer the crude dibromide to a separatory funnel which has a properly lubricated stopcock. Shake the stoppered funnel *very gently*, and relieve gas pressure as described in § 88. Wash the product first with water. If it is thought that any bromine persists, wash with a few cubic centimeters of dilute sodium bisulfite solution. Next wash with sodium hydroxide (about $N/2$) and finally with water again. Separate the product carefully, transfer to a small conical flask, dry over granular anhydrous calcium chloride, and distil over wire gauze. Yield, 30 g. Boiling point of pure propylene dibromide, 141.6°.

226. Liquid Propylene. If a low-range thermometer and solid carbon dioxide are available, an interesting extension of this experiment may be arranged by condensing a small quantity of the

propylene (b. pt. −47°).   A small (4- or 5-inch) test tube, fitted like the 8-inch test tube shown in the illustration, is stood in a mixture of coarsely crushed solid carbon dioxide (dry ice) and alcohol contained in a 250-cc. beaker nested in a 400-cc. beaker.   An effective ice-salt mixture in the filter flask is essential here.

After a quantity of liquid propylene has been condensed, the test tube is removed from the alcohol bath, the thermometer is inserted, and the propylene is allowed to boil spontaneously (no flames!) for determination of boiling point.   Any residue of propylene may be used to react with aqueous potassium permanganate, illustrating Baeyer's test for the double bond.

Optional Syntheses

227. Ethylene and Ethylene Dibromide.   Prepared in a similar manner, but requiring concentrated sulfuric acid as reagent, and a sodium hydroxide wash instead of ice-salt (Refs. 23, 24, 26, 27, 30, 33, 34, 35, 37, 38, 39, 40, 41, 43, 45).   See also *J. Chem. Education* **13,** 377 (1936).

228. Cyclohexene. An alkene is prepared from a cycloalkanol (Ref. 23).

Questions

1. Explain how an ether might be produced as a by-product in this experiment.

2. How could you tell that the reaction of propylene with bromine was not one of substitution?

3. Suppose that isopropyl alcohol through neglect were allowed to reach the bromine.   What undesirable product might then be produced?

4. Why would one expect the product cited in question 3 to be noxious?

5. Suppose that methyl alcohol were substituted for the isopropyl alcohol.   What organic product would you expect?

6. What chemistry is involved in the use of the sodium hydroxide at the end of the apparatus where the waste vapors escape?

7. What other methods could be used to produce the propylene?

8. What is the purpose of the long "safety" tube?

9. Suppose you desired to prepare hexene instead of propylene.   What changes would you expect to make in the directions?

10. Suppose you substituted a tertiary alcohol for the isopropyl alcohol. Would this substitution have any effect on the readiness with which the reaction would take place?   What change in the directions would you make?

11. Why does the propylene dissolve in the bromine more freely after the reaction has proceeded for some time?   (See § 133.)

EXPERIMENT 11

Amylene and Acetylene

229. Advantage is taken of the comparative ease with which a tertiary alcohol is converted into the corresponding alkene as suggested in § 225. Where more than four carbon atoms are present in the molecule, more than one alkene may be derived from a single experiment. The slightly ambiguous commercial name "amylene" is given to the mixture of isomeric pentenes obtained in the reaction described below.

$$\begin{array}{c} CH_3 \\ | \\ CH_3-C-CH_2-CH_3 \rightarrow \\ | \\ OH \end{array}$$

$$\begin{array}{cc} CH_3 & CH_3 \\ | & | \\ CH_3-C{=}CH-CH_3 + CH_2{=}C-CH_2-CH_3 \end{array}$$
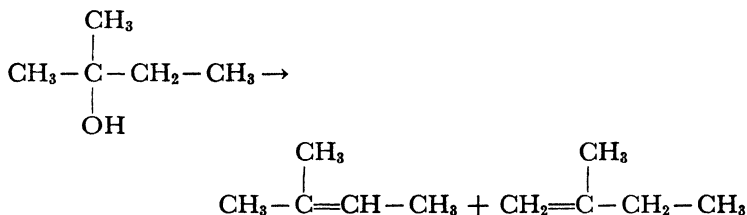
In the second part of the experiment the well-known salt of acetylene, commercial calcium carbide, is treated with water, which causes rapid hydrolysis and evolution of the desired gaseous product. Acetylene, a triply-bonded compound, is thus regarded as a weak acid, playing a role unusual for a hydrocarbon. For such a role the triple bond alone is not sufficient. There must be hydrogen attached to at least one of the triply bonded carbon atoms.

$$CaC_2 + 2H_2O \rightarrow C_2H_2 + Ca(OH)_2$$
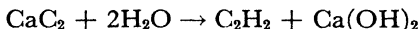
230. Amylene. The isomeric products from this experiment have boiling points only slightly higher than that of ordinary ether, and should be treated with the same attention to fire hazards which is required with ether. (See § 34.)

Attach a Hempel fractionating column to a 500-cc. round-bottomed flask, fit a thermometer (110° range) to the top of the column, and connect the delivery tube to a water-jacketed condenser. Inasmuch as the product of this experiment is a very volatile liquid,

it is desirable to avoid pouring it out later when a record of yield is to be made. Accordingly, weigh the clean dry receiver (a 100-cc. conical flask) in advance, and set it in a large beaker of crushed ice and water. A bent adapter, attached to the condenser, facilitates passage of the distillate into the receiver with minimum loss.

With stirring, cautiously add 25 cc. of conc. sulfuric acid to 40 cc. of water in a small beaker. Cool the solution, place in the 500-cc. flask of the apparatus above described, and add 40 cc. of tertiary amyl alcohol.

Heat the reaction mixture gently, preferably in a steam cone. If care is taken to have all corked openings secure and the receiver well cooled in ice, the ordinary arrangement over wire gauze will do. Regulate the heat so that the temperature of the vapors at the top of the column does not exceed 40°. Stop the distillation when no more distillate can be sent over without exceeding this temperature. Remove the receiver, wipe the outside with a towel, and weigh. Calculate the yield of crude amylene. Dry the preparation over about 2 g. of anhydrous calcium chloride or magnesium sulfate, using the original conical flask. Stopper the flask securely, on account of volatility, for use later in § 232. Yield, 15 g.

231. Acetylene. Assemble the acetylene generator as described below, but do not proceed to the actual production of the gas until the amylene has been prepared and there is time (1 to 2 hours) to complete the experiment.

Fit a small dropping funnel to a 100- or 125-cc. distilling flask containing about 10 g. of calcium carbide. See that the stopcock is properly lubricated and in good working order. Very cautiously drop water from the funnel upon the carbide, thus generating acetylene gas.

Pass the acetylene through a wide-mouthed safety bottle and thence to a pan of water or a pneumatic trough, where it can be collected by downward displacement. Fill a small test tube, two narrow-mouthed bottles, and a wide-mouthed bottle *in the order named,* and proceed to § 232 (*a*) at once.

COMPARISON OF AMYLENE AND ACETYLENE

232. (*a*) *Reaction with Ammoniacal Cuprous Chloride.* Dissolve 0.5 g. of cuprous chloride in 5 cc. of ammonium hydroxide and dilute to

20 cc. (Be sure to leave the cuprous chloride bottle well stoppered after use, to prevent oxidation.)

(1) Pass acetylene into 10 cc. of the cuprous chloride solution. Collect the precipitate on a Buechner filter (see § 95) and dry it between filter papers. Explode it by heating small pieces in a flame.

(2) Treat about 2 cc. of amylene with cuprous chloride solution. Test petroleum ether in the same manner.

(*b*) *Reaction with Ammoniacal Silver Nitrate.* Add dilute (N) ammonium hydroxide drop by drop to 1 cc. of N/10 silver nitrate solution until the precipitate which forms just redissolves, then add water to bring the volume to 6 cc.

Add one-half of the silver solution to a test tube of acetylene gas, and the other half to a test tube containing 1 cc. of amylene. Filter; wash and dry any precipitate forming. Explode by heating small pieces in a flame.

Note: Before leaving the laboratory, destroy all the remaining silver precipitates and any ammoniacal silver solution by warming the material with dilute hydrochloric acid.

(*c*) *Combustion.* (Out of doors or in a hood.)

(1) Burn 1 cc. of amylene in an evaporating dish.

(2) Ignite the acetylene in the wide-mouthed bottle. Compare the luminosity of the two flames and record any other differences which you observe.

(*d*) *Reaction with Bromine.*

(1) Shake a mixture of 2 cc. of bromine water with 1 cc. of amylene in a test tube.

(2) Add 2 cc. of bromine water to one of the narrow-mouthed bottles of acetylene and shake. Compare results.

(*e*) *Reaction with Permanganate.*

(1) To the other narrow-mouthed bottle of acetylene add 1 cc. of a very dilute solution of potassium permanganate. Shake well and record results.

(2) Try a similar experiment with amylene.

Optional Synthesis

233. Butenes. When sec-butyl alcohol is used as a source of an alkene, a mixture of the cis- and trans-isomers of 2-butene is produced. This is an extremely volatile liquid, boiling range approx. 0° to 3° C. If not converted at once into other substances, the butene mixture must be condensed with ice

and salt, or solid carbon dioxide, and sealed.   (Note precautions mentioned in § 223.)

Questions

1. From which alcohol may an alkene be most readily prepared—primary, secondary, or tertiary?

2. Why do we not purify the amylene chemically as we do ethylene?

3. Give a satisfactory name for each of the isomeric pentenes prepared in this experiment.

4. What isomeric amylene dibromides might be present in the reaction products from amylene and bromine?   Which one would likely predominate?   Why?

5. Write the equation for the transformation of calcium carbide into acetylene.   Does this reaction run to completion?   Why?

6. How do you explain the formation of silver acetylide?   What is the purpose of the ammonium hydroxide in the experiment?

7. Is the ionization constant of acetylene greater than that of water?   How can you tell?

EXPERIMENT 12

Diethyl Ether

$$C_2H_5HSO_4 + C_2H_5OH \rightarrow C_2H_5OC_2H_5 + H_2SO_4$$
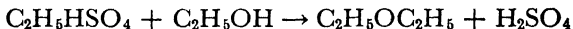
234. Ethyl sulfuric acid, prepared by mixing ethyl alcohol with sulfuric acid, as is heated with a second equivalent of ethyl alcohol. The temperature is lower than that required for ethylene, and a dialkyl oxide, or ether, is produced.

In a 500-cc. distilling flask place 60 cc. of 95% ethyl alcohol, and slowly add with effective shaking 60 cc. of concentrated sulfuric acid. Mount this flask over wire gauze in the manner shown in the accompanying diagram. Attach to it the longest water-cooled condenser available, and place a mixture of ice and salt in the beaker holding the receiver. The receiver should be of about 250 cc. size, preferably with short neck. Attach a high-range (0° to 360°) thermometer and dropping funnel as shown, and use a tube of small bore (about 1.5 mm. inside diameter) leading from the delivery tube of the dropping funnel. The restricted bore prevents bubbles from rising in the stem and interfering with the flow of liquid. In the absence of commercial capillary tubing of the bore specified, a substitute may be prepared by drawing down the lower end of a suitable length of heavy-walled 6- or 7-mm. common glass tubing. The rubber tube connected to the receiver hangs over the edge of the desk as a safety precaution. (See § 34 (b).)

A dropping funnel with short delivery stem is more convenient than the device pictured. The illustration merely demonstrates that it is not necessary to cut off the stem of the standard commercial funnel and render the piece unsuitable for other purposes.

Heat the reaction mixture to 140° and run into it gradually an additional 125 cc. of ethyl alcohol as fast as the ether collects in the receiver. The temperature should be kept between 140° and 150°. Continue heating for 5 to 10 minutes after the last of the alcohol has been added, but do not allow the temperature to exceed 160°.

With the aid of a common ring, mount a small separatory funnel on a stand, and see that all paper strips are removed from the ground-glass stopper and the stopcock plug. Treat the latter with a small quantity of stopcock lubricant. To this funnel transfer the crude ethereal distillate. Noting the procedures described in § 87, wash the crude ether product with *ice-cold* wash liquids, as follows:
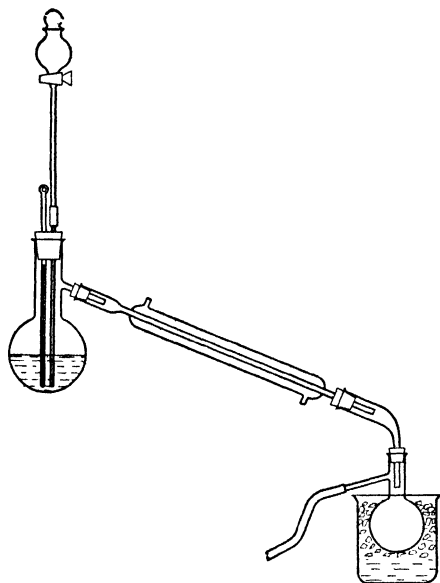
25 cc. of 3N sodium hydroxide, then with about 20 cc. of water, and finally with a volume of saturated calcium chloride solution about equal to that of the remaining ether. Noting methods described in § 112, dry the ether over calcium chloride (about 10 g.) for a day or more. Stopper the drying flask securely, since ether is very volatile.

At the next laboratory hour decant the ether from the mass of partially hydrated calcium chloride through a funnel into a small distilling flask. Now mount the distilling flask in a cool water bath, and connect with the water-cooled condenser and receiver in ice, as shown above. Distil the ether with careful attention to fire hazards, collecting the fraction passing over between 33° and 38°. Higher-boiling material contains an excessively large fraction of alcohol. Yield, 50 g. Boiling point of pure ether, 34.5°.

Optional Syntheses

235. Dibutyl Ether (Ref. 25). **Unsymmetrical Ethers.** Ethers in which two different radicals are attached to oxygen are prepared in the laboratory with the aid of an alkyl halide and a sodium alkylate—for example, ethyl amyl ethers (Refs. 24, 39), and phenetole, $C_6H_5OC_2H_5$ (Refs. 26, 30, 37, 38, 43, 45).

Questions

1. Which is denser, ether vapor or carbon dioxide?

2. Why is it not satisfactory to use the sulfuric acid process to produce "mixed" or unsymmetrical ethers?

3. Write an equation showing how dimethyl sulfate and an alcohol might be used to prepare an ether.

EXPERIMENT 13

Propionaldehyde

Oxidizing and Reducing Agents, $Cr_2O_7^=$ and C_3H_7OH
Reduced and Oxidized Products, Cr^{+++} and C_2H_5CHO

236. The interaction of a primary alcohol, such as *n*-propyl alcohol, with a suitable oxidizing agent, such as a dichromate, proceeds rapidly provided the acidity of the mixture is high. Accordingly, in this experiment alcohol, a dichromate, and sulfuric acid are mixed. The aldehyde, presumably the first and normal product of oxidation, is then isolated as soon as possible by distillation. In view of the possibility that aldehyde may be oxidized still further, special care is taken in manipulation to reduce that possibility to a minimum.

The whole quantity of alcohol, dichromate, and acid should not be mixed in advance, lest a violent reaction take place. It is necessary to make the mixture gradually. On the other hand, any two of the three reagents may be mixed in quantity beforehand without any such violent reaction. It is therefore convenient to mix two, and gradually add the third—or reverse the order of addition. With the apparatus pictured below six arrangements are thus possible, as follows:

1. Drop mixture of **alcohol** and **dichromate** into **acid.**
2. Drop mixture of **alcohol** and **acid** into **dichromate.**
3. Drop mixture of **dichromate** and **acid** into **alcohol.**
4. Drop **acid** into mixture of **alcohol** and **dichromate.**
5. Drop **dichromate** into mixture of **alcohol** and **acid.**
6. Drop **alcohol** into mixture of **dichromate** and **acid.**

A decision is now made as to the most promising of the six plans; or if two or more seem suitable, different students may try different arrangements.

Assemble the apparatus as shown below, noting that the funnel is connected as closely as possible by rubber tubing to a piece of 6-mm. glass tubing drawn to a capillary tip about 1 mm. in di-

ameter. The receiver should be immersed in a mixture of water and finely crushed ice.

In 200 cc. of water dissolve a quantity of either anhydrous sodium dichromate, or the hydrate ($Na_2Cr_2O_7.2H_2O$), 3% in excess of the theoretical requirement to convert 0.7 mole of n-propyl alcohol into aldehyde. (See § 30 for discussion of method of calculation.)
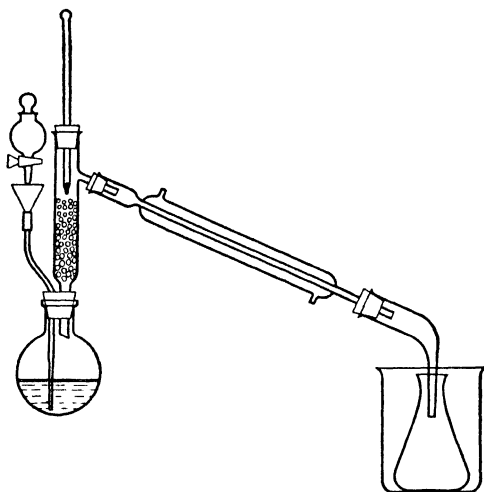
The second solution is prepared by carefully pouring 55 cc. of conc. sulfuric acid into 100 cc. of water in a flask or beaker, and cooling. The third reagent is 0.7 mole of n-propyl alcohol.

Following the chosen plan, mix the proper two reagents, and place the mixture either in the dropping funnel or the generator flask, as required. The third reagent is then placed in the other vessel.

Heat the liquid in the flask until it boils, and until the main current of hot vapors reaches the lowest beads in the fractionating column. Now start dropping in the liquid from the funnel at a rate about 30 to 40 drops per minute. The resulting oxidation, which proceeds at once, produces so much heat that propionaldehyde is distilled promptly. Comparatively little aid from the burner is now required. The temperature should not exceed 60° at the top of the column; otherwise an excessive amount of unchanged alcohol is likely to escape from the reaction zone. The experiment now be-

comes virtually a small-scale engineering feat, in which rate of dropping and intensity of the flame are controlled with constant watching of the thermometer. As the oxidation proceeds, more and more dependence must be placed on the external heating; notice, however, that there is a time lag between change of heating and corresponding effect at the top of the column. Finally at the close allow the temperature to rise slowly to 70°.

Dry the distillate for an hour or more over a suitable neutral drying agent. About 3 to 4 g. of anhydrous magnesium sulfate is suitable. Filter through a very small piece of cotton in a funnel, and distil through the Hempel column into a receiver placed in ice water. The fraction collected below 55° is preserved as the preparation of propionaldehyde. Boiling point when pure, 48.8°. Yield, 30%.

237. Tests. Silver Mirror. A test tube is thoroughly scrubbed with household washing powder and rinsed with clean water. In this clean, wet test tube are placed about 10 cc. of dilute (0.05 N) silver nitrate, one drop of 6N sodium hydroxide, and just enough aqueous ammonia added drop by drop to redissolve the precipitate first formed. If a drop of propionaldehyde is added to this mixture, metallic silver will soon be precipitated. Should the mixture be too warm or too concentrated, the silver will fall as a muddy precipitate all through the solution. If favorable conditions are chosen, a beautiful silver mirror will be deposited on the test tube. The reaction mixture may require slight warming. After the experiment, discard the ammoniacal silver solution at once, as it tends to produce an explosive silver-nitrogen compound. (See also § 274 (a).)

238. Fehling's Test. Propionaldehyde also gives Fehling's test for aldehydes. A few drops of the aldehyde are heated with a freshly prepared mixture of equal volumes of Fehling's solutions "No. 1" and "No. 2," yielding a bright red precipitate of cuprous oxide. (See also § 274 (b).)

Optional Syntheses

239. Acetaldehyde. From ethyl alcohol. Since this aldehyde is extremely volatile (b. pt. 21°), it is usually the custom to convert the newly prepared aldehyde vapor directly into the crystalline addition compound with ammonia.

240. Benzaldehyde. The simplest aldehyde of the aromatic series; constituent of almond oil (Refs. 27, 28, 30, 32, 34, 35, 37, 40, 43).

Questions

1. Why does not the dichromate oxidize the alcohol without the aid of sulfuric acid?

2. Why did you choose the particular plan of admixture used by you?

3. Which of the six plans of admixture of reagents do you think to be the worst of the lot? Why?

4. Which do you think would be the best of the plans which were not used?

5. Why are such pains taken to have the distillation proceed on prompt and regular schedule?

6. Suppose you wished to prepare *n*-valeraldehyde (pentanoic aldehyde) by an experiment of this type. What new difficulties might arise? (Consider boiling point and solubility relations.)

EXPERIMENT 14

Acetone: Use of the Fractionating Column

Oxidizing and Reducing Agents, $Cr_2O_7^-$ and $CH_3.CHOH.CH_3$
Reduced and Oxidized Products, Cr^{+++} and $CH_3.CO.CH_3$

241. In the presence of strong acid a dichromate will oxidize a secondary alcohol to the corresponding ketone. If care is taken to maintain an excess of alcohol over oxidizing agent during most of the reaction period, oxidation of the ketone itself is largely prevented. In the present case the temperature is kept low until practically all of the alcohol has been consumed, and then only two volatile components remain—ketone and water. A simple distillation yields a mixture of these two free from undesired salts, ready for the principal part of this experiment, namely, the distillation of one particular mixture by two different methods. (See §§ 60 and 74 for theory of these operations.)

In view of the fact that acetone is not only volatile but subject to side reactions, it is essential that this experiment be not interrupted while the ketone product is still in contact with the acid-chromic salt mixture; that is, the whole procedure of § 242 should be carried out continuously. It is still better to complete the entire experiment in one day.

To a 700- or 1000-cc. Florence flask containing 25 cc. of water add carefully, with shaking, 50 cc. of conc. sulfuric acid. Cool the flask under the tap; then add 100 cc. of water and 0.5 mole of isopropyl alcohol. Be careful to note whether anhydrous or aqueous alcohol is furnished. Commercial isopropyl alcohol varies from nearly pure anhydrous material to the constant-boiling aqueous mixture containing approximately 12.5% of water. Make whatever allowance is necessary in your calculations.

Provide an ice bath of size large enough to permit the complete immersion of the body of the flask. This bath should contain at least 500 g. of finely crushed ice, together with enough water to form a thin slush which will readily allow the entrance and removal of the flask from time to time in the later procedures. In a small beaker

203

containing 25 cc. of warm water dissolve that quantity of sodium dichromate (anhydrous or dihydrate) which will be about 3% in excess of the amount required by theory to convert the alcohol into the ketone. For method of calculation see § 30.

A thermometer is now mounted in the flask in such a manner that it is held rigidly, with its bulb in the reaction mixture, but with some arrangement for adding a liquid reagent from time to time. An old common cork, bored somewhat off center to receive the thermometer and with one side cut off, will be satisfactory.

242. Oxidation. Immerse the flask in the ice bath, and add the dichromate solution in from 10 to 15 portions. After each addition shake the vessel for a moment in the open with a gentle rotary motion, and immediately plunge it into the ice bath. If the temperature threatens to rise above 40°, remove the flask from the bath, shake again, and return promptly to the ice bath. As soon as the temperature falls to 25°, add a new portion of dichromate. Do not try to lower the temperature below 25°, lest the oxidation be held up and a large amount of unreacted material accumulate, ready to undergo too vigorous a reaction when the temperature is allowed to rise again. At the end of this operation the color of the mixture should be green, as of chromic salts, possibly with a slight olive or yellowish tint indicating indirectly that no more alcohol is left to react.

When the temperature of the reaction mixture shows no further tendency to rise spontaneously, transfer the material to a 500-cc. distilling flask and add boiling stones. Distil through a water-cooled condenser into a 100- or 125-cc. distilling flask used as receiver. After the temperature of distillation reaches the boiling point of water, continue distilling until about 10 cc. more of liquid comes over at this (constant) temperature. Now discard the dark-colored aqueous residue.

243. Fractionation. The distillate obtained is a mixture of the desired ketone with water. The *entire quantity* of this product is now to be distilled by the simple method (*a*) from an ordinary distilling flask. The product from method (*a*), which is presumably identical with the liquid from which it came, is redistilled by method (*b*), with use of a fractionating column. Since the main purpose of the

experiment is to distil identical mixtures by two methods, *no rejection of any part of the boiler contents is permissible in either the (a) or (b) procedure.*

Method (a). Attach the distilling flask, with its accumulation of crude aqueous acetone and some fresh boiling stones, to the condenser, and provide a bent adapter to convey the new distillate to a 50- or 100-cc. graduated cylinder, which is to be used as receiver. In warm weather it may be well to stand this cylinder in ice water. Do not allow the liquid to drop through the open air and thus suffer evaporation.

Now distil at a steady, uniform rate the entire contents of the flask, and record in the notebook the *boiling point* and *yield so far collected* at each 2 or 3 cc. interval. In spite of all care, a few drops of less volatile liquid will always be found as a residue in the distilling flask after the apparatus has become cool. Investigate this material, and test your prediction as to its identity. Is it pure water?

Method (b). Transfer the distillate in the graduated cylinder to a 200-cc. round-bottomed flask to which is fitted a fractionating column. From this flask and column redistil the aqueous ketone solution slowly (1 to 2 drops per second), making a record of temperature and yields as in the previous distillation. There must be no interruption of the distillation while these data are being taken. Watch out particularly for drafts in the laboratory which cause irregular cooling of the column. Any fall in temperature is prima facie evidence that the apparatus is not being manipulated properly.

As the rate of distillation falls, gradually heat the flask more strongly. Soon the temperature will rise suddenly. When it reaches 65°, change receivers. A test tube or small flask will serve as receiver until the graduated cylinder is again available. Preserve the main distillate as your acetone preparation. Continue the distillation with its accompanying periodic records until you can get no more liquid to go over into the receiver.

Draw on one graph the two curves representing the two distillations—with and without the fractionating column. On this graph plot the boiling points as ordinates, and yield in cubic centimeters as abscissas. Either draw this diagram in the notebook, or prepare it on a small piece of cross-sectional paper and paste it in the notebook. Yield of acetone, 32 cc.

Optional Syntheses

244. Methyl Ethyl Ketone (Butanone). If the isopropyl alcohol of the above experiment is replaced with *sec*-butyl alcohol (2-butanol), methyl ethyl ketone is produced. The reaction and distillations proceed in similar manner. In this case, however, there is a sharp deviation from Raoult's law, leading to an interesting example of partial miscibility and a low constant boiling point of the aqueous mixture. (See, *J. Chem. Soc.*, **89**, 1375 (1906), for particulars.) Incidentally, the slight discoloration often occurring in preparations of this compound is readily eliminated by the addition of 1 to 2 g. of solid sodium hydroxide to the ketone just before its last distillation. (See also Ref. 25.)

Diethyl Ketone may be prepared in somewhat analogous manner from diethyl carbinol.

Acetone may be prepared by the classical dry-distillation method, employing a salt of acetic acid (Refs. 27, 28, 30, 39, 40, 41, 43, 45).

Questions

1. What is the green substance produced in this reaction?
2. What is the purpose of the sulfuric acid?
3. Why do the distillation curves differ in form?
4. What would be an ideal curve for distillation of this mixture?
5. Suppose an excess of dichromate were added. What new products might then be expected in quantity?
6. What answer would you give to question 5 if secondary amyl alcohol (3-pentanol) instead of secondary propyl or butyl had been used?

EXPERIMENT 15

The Haloform Reaction

245. A methyl ketone (CH_3COR), such as acetone, reacts with either hypochlorite, hypobromite, or hypoiodite in such a manner that the three hydrogen atoms on the methyl group are replaced by halogen atoms. The resulting trihaloketone immediately hydrolyzes, yielding a compound of type formula CHX_3. When hypochlorite is used, chloroform, $CHCl_3$, is produced, as indicated in the following summary of the process as applied to acetone.

$$CH_3COCH_3 + OCl^- \rightarrow$$
$$CHCl_3 + CH_3COO^- \text{ (acetate ion)} + Cl^- + H_2O$$

Similarly, bromoform and iodoform are obtained from hypobromite and hypoiodite. These latter hypohalite reagents are not stable and well defined, however, and are thus not obtainable as commercial reagents. They are instead freshly prepared as needed.

246. Chloroform. To 3 cc. of acetone in a 6-inch test tube add 15 cc. of fresh household bleaching solution (Clorox, Purex, or other commercial sodium hypochlorite solution, approximately 5%). Mix well. A turbid emulsion of chloroform in the aqueous solution is produced. The crude chloroform may float at first on account of the appreciable amount of less dense acetone which it extracts. After occasional shaking, the denser chloroform sinks and slowly accumulates at the bottom of the test tube. Allow to stand for 15 minutes or more and start the next experiment. The yield is very small, so no attempt is made to turn out a purified product.

Wash the accumulation of chloroform by introducing into the test tube a small tube from which a slow trickle of cold water is running, and allow the supernatant hypochlorite solution to overflow into the sink. Finally leave the test tube about half full of the last wash water introduced, with the globule of chloroform at the bottom. Add one or two drops of iodine-iodide solution. Shake the mixture gently and allow the chloroform to sink again. Note the ability of the chloroform to extract iodine in the violet form.

247. Bromoform. In a 300- or 500-cc. flask place about 150 g. of crushed ice and 4 cc. of liquid bromine. (Be careful in handling dangerous bromine; see § 225.) Provide 55 cc. of 3N sodium hydroxide solution ready for use. Add 10 cc. of acetone to the bromine-ice mixture, and immediately start adding the sodium hydroxide in small portions with shaking. The addition should be complete in about 3 minutes, while the reaction mixture, dark at first, gradually becomes white or nearly so. Allow the resulting emulsion to stand for a few minutes, during which time the bromoform settles to the bottom of the flask. Wash by decantation (see § 246), and separate the bromoform in a small separatory funnel. Run the wet bromoform into a small test tube and carefully heat to the boiling point, thus expelling a residue of acetone. Cool the tube under the faucet, and then in the ice bath. Bromoform crystallizes in shining leaflets, m. pt. 7°. No further attempt is made to purify the product unless semimicro apparatus is available (Ref. 25). If the compound is prepared in larger quantity, it may be dried over calcium chloride and distilled over wire gauze; b. pt. 150°.

248. Iodoform. In a 500-cc. flask dissolve 5 g. of potassium iodide in 100 cc. of water, and add 2 cc. of acetone. Slowly add, with shaking, household bleaching solution (see § 246) until no further precipitate of iodoform is produced. Collect the precipitate on a suction filter, wash with cold water, suck the mass as dry as possible, and recrystallize under reflux condenser (§ 101) from ethyl alcohol. Yield, 3 g. Melting point of pure iodoform, 119°.

Questions

1. Write complete equations for the succession of reactions in each of the three foregoing cases, starting with chlorine, bromine, and iodine in the forms used in our experiment.

2. Write equations showing how iodoform might be obtained from (*a*) methyl amyl ketone, (*b*) ethyl alcohol, starting with free iodine in each case.

3. What yield of chloroform is theoretically obtainable from 35.46 g. of chlorine?

4. What substance would be produced by the hydrolysis of chloroform?

5. The melting point of bromoform is almost as high in the presence of water as when dry, whereas the difference in the case of phenol is much greater. Explain on the basis of melting-point theory.

EXPERIMENT 16

Glacial Acetic Acid

$$CH_3COONa + H_2SO_4 \rightarrow CH_3COOH + NaHSO_4$$
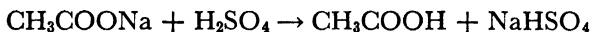
249. When a strong acid is mixed with the salt of a much weaker acid, the free weak acid is produced. Acetic, propionic, butyric, etc., acids may thus be readily prepared.

In a distilling flask of from 100 to 250 cc. capacity place 40 g. of coarsely powdered anhydrous sodium acetate (see note below). Using a long-stemmed funnel to prevent wetting the neck of the flask, add cautiously 25 cc. of conc. sulfuric acid. If the mixture becomes so hot that loss of vapors is threatened, cool the flask in tap water.

Attach a thermometer and water-cooled condenser in the manner customary for distillation, and heat the flask over the wire gauze. The distillate is glacial acetic acid. A very careful worker, using clean apparatus, will obtain a good product directly from this distillation. Often it is necessary to redistil the product. For this purpose a 50-cc. distilling flask is appropriate, or the one first used may be cleaned and dried for the purpose.

(*Note.* Commercial sodium acetate of the so-called "anhydrous" grade always contains more or less water. It may be rendered anhydrous by being heated cautiously in an evaporating dish of ample size, or a clean iron pan. Stir the melted salt until the water vapor has been expelled, but avoid overheating. Allow the mass to cool, and when solid grind in a mortar.)

250. Purity of the Acid. The principal impurity in the acid is water. As water lowers the melting point of acetic acid markedly, a determination of this constant serves as a method of analysis.

Place the whole quantity of acetic acid as prepared above in a clean, dry 8-inch test tube. (See that the test tube is well made, with a sound bottom, and is not cracked or in any way likely to

break when used in this experiment.)   Insert a clean dry ther-
mometer in the acid, and place the outfit in a bath of finely crushed
ice and water.   If the product contains much water, it will be neces-
sary to add a little salt to the ice.

Stir the acetic acid gently with the thermometer until it freezes.
Probably it will be necessary to undercool the liquid many degrees
before it will start to crystallize.   When crystallization starts, remove
the tube from the cooling bath.   Continue stirring, and note the
temperature when the last few crystals are just about to disappear.
This temperature is the so-called "melting point" of the preparation.
Consult the table in the Appendix (§ 448) which shows the per-
centages of acid corresponding to various melting points; also see
§ 160.   Yield, 22 to 24 cc.

Questions

1. What fundamental principle of general chemistry would lead one to
expect an acid such as sulfuric to react with the salt of an organic acid?   Ex-
plain in terms of chemical equilibrium.

2. What change of technique and reagents would you make if you were
trying to get oxalic acid from its salt, instead of acetic acid from sodium
acetate?

3. At the time when you had part crystals and part liquid during the
melting-point test, what was the difference in composition between the
solid and the liquid?

4. Why do we not record the temperature when melting *starts*, instead of
that when it just ends?

5. Why does the melting point of acetic acid fall so rapidly when *water* is
added as an impurity?

6. What objection might there be to the substitution of hydrochloric acid
for sulfuric acid in this experiment?

EXPERIMENT 17

Acetyl Chloride

$$PCl_3 + 3CH_3COOH \rightarrow 3CH_3COCl + P(OH)_3$$
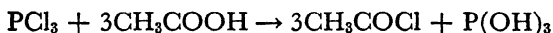
251. Either phosphorus trichloride or pentachloride normally converts a carboxylic acid into the corresponding acid chloride. Although much phosphorous acid $[P(OH)_3$, or $H_3PO_3]$ is formed in the case of the trichloride, there may also be produced certain less hydrated forms of that acid, also mixed anhydrides, as suggested in the experimental directions below. Such by-products are of necessity accompanied by considerable gaseous hydrogen chloride, which is absorbed in water so as to prevent a laboratory nuisance.
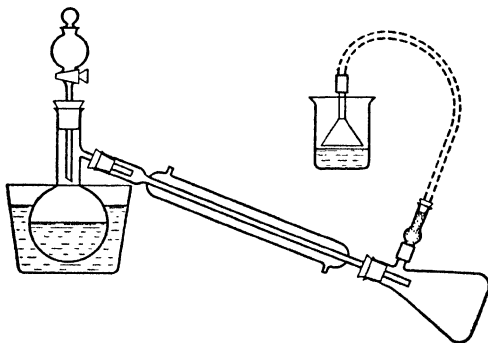
Arrange apparatus according to the above illustration, including a 500-cc. distilling flask which holds a dropping funnel and is cooled with ordinary faucet water. The condenser is firmly attached to a 500-cc. filter flask carrying a calcium chloride tube and a funnel which approaches *but does not touch* the solution (1N sodium hydroxide) in the beaker. **Warning.** If the solution in the beaker should be permitted to be sucked back into the flask, the acetyl chloride will be hydrolyzed so rapidly, and with so much evolution of heat and resulting vapors, that a serious explosion is likely to occur. Even common water, as well as the sodium hydroxide, will cause such an

explosion. See that the flask is in good condition, without crack, and that it is mounted without mechanical strain on the sidestem; and mount the funnel securely.

Place 1 mole of glacial acetic acid in the distilling flask, and add, in small portions, 0.4 mole of phosphorus trichloride through the funnel. Note that phosphorus trichloride is a very offensive substance. Do not pour it out of any vessel except under protection of a hood, or out of doors. Be especially careful not to throw either phosphorus or acetyl chloride into a sink in the laboratory.

As soon as the trichloride has all been added to the acetic acid in the flask, gently heat the water bath to 50°. The reaction mixture soon separates into two layers, indicating that the reaction is nearly complete. Continue to hold the temperature at about 50°, if necessary, until the desired separation occurs. Now heat the water to boiling, and distil the crude acetyl chloride until no more liquid passes over. (*Note.* Do not attempt to obtain a larger yield by removing the water bath in order to heat the flask in the open. It is reported that such attempts may lead to the formation of some unknown explosive substance.) Pour out the sirupy residue of phosphorous acid into a bottle provided for the purpose in the laboratory.

To the crude acetyl chloride add 2 drops of glacial acetic acid and redistil. Collect the distillate coming over at temperatures below 57°. Take the receiver containing the final product outdoors or to a hood, and transfer the liquid either to a glass-stoppered bottle or to such other container as the instructor designates. Neither rubber stoppers nor corks are admissible here. Yield, 50 g. Boiling point of pure acetyl chloride, 52°.

Acetyl chloride made by this method contains a very small amount of some volatile phosphorus compound which causes a white precipitate to appear in the final product after it stands a few days. This volatile compound may be residual phosphorus trichloride, or possibly phosphorus dichloride monoacetate ($CH_3CO.O.PCl_2$). It is not necessary to remove the white precipitate before practical use of the acetyl chloride preparation.

Optional Syntheses

252. Benzoyl Chloride. A valuable laboratory reagent, whose preparation illustrates the use of phosphorus pentachloride instead of trichloride.

The experiment also gives a good illustration of fractional distillation of a mixture of two liquids (benzoyl chloride and the by-product phosphorus oxychloride). It should not be attempted without good facilities for ventilation (Refs. 27, 29, 30, 32, 34, 35, 38, 40, 43).

p-Nitrobenzoyl chloride. A solid acid chloride (Refs. 3, 6, 24, 26, 27).
Conversion of acetyl chloride into an ester. (See § 257.)
n-Butyryl chloride. Illustration of the use of thionyl chloride (Ref. 9).

Questions

1. What products are formed in the possible serious explosion referred to in the description of apparatus given above?

2. Why is "glacial" acetic acid preferred to dilute acid?

3. Why does the product start to boil before its temperature reaches 52°? Why does the boiling temperature rise above 52°?

4. Why do you not dry this preparation with calcium chloride or similar drying agent?

5. Of what practical value is this type of acid derivative?

6. Devise apparatus for the conversion of acetyl chloride into ethyl acetate, knowing that ethyl alcohol and acetyl chloride react with each other vigorously.

7. Can you offer any argument which might reasonably explain why the reaction mixture first exists in one phase, but separates into two phases later on in the experiment? (This question presupposes class discussion on solubility of organic substances.)

8. Why should it be necessary to distil this preparation a second time when it has already been distilled in clean apparatus in the first operation?

9. Suppose you had occasion to prepare both volatile, liquid acid chlorides and involatile, solid acid chlorides. Would these differences have any bearing on your choice of phosphorus pentachloride in some cases instead of trichloride?

EXPERIMENT 18

Acetic Anhydride

$$CH_3COCl + CH_3COONa \rightarrow CH_3CO.O.COCH_3 + NaCl$$
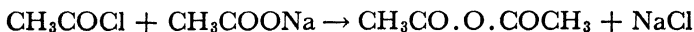
253. Through union of the "acetyl" and "acetate" radicals of the starting materials shown above, an acid anhydride is formed. It is essential not only that the sodium salt be thoroughly dried, but that the acyl halide reagent be allowed adequate time to penetrate the granular solid mass of that salt before final distillation occurs.

The laboratory supply of anhydrous sodium acetate is tested for water content by heating a sample in a small test tube. If the material gives off an appreciable amount of water, the quantity to be used in this experiment should be freed from water by the method described in the directions for acetic acid, § 249.

Mount a 500-cc. distilling flask, fitted with a dropping funnel and a water-cooled condenser as shown in Fig. 4, § 33, but without wire gauze or other support below the flask. Provide a 100- or 125-cc. distilling flask as receiver. Place 60 g. of pulverized anhydrous sodium acetate in the flask, and run in slowly 0.6 mole of acetyl chloride. In spite of the most careful control of the reaction the mixture will probably become hot enough to drive over a little unchanged acetyl chloride into the receiver. Such premature distillate should be returned to the distilling flask through the funnel.

With the aid of a stout stirring rod mix the reacting materials as thoroughly as possible. Now replace the dropping funnel with a thermometer and cork, and distil the acetic anhydride with a large, quiet blue flame played over the bulb of the flask. Care must be taken not to heat the flask to redness at any point. (In eastern laboratories, where domestic gas contains much free hydrogen, particular pains should be taken not to operate the burner at high efficiency. The air ports should be so nearly closed that the flame shows a slightly yellow tinge without being sooty. With natural gas

less trouble is encountered. Some writers recommend a yellow flame with a hot-burning fuel such as coal gas.)

Add about 2 to 3 g. of finely powdered sodium acetate to the crude distillate and redistil. Collect that portion of the distillate near to the boiling point of pure acetic anhydride, 140°. If a large fraction of the product comes over at temperatures much below 140°, redistil. By this time the major residual impurity will probably be acetic acid, b. pt. 118°. A range of 135° to 140° is acceptable; for some purposes, where a little more acetic acid is not harmful, the initial figure may be taken at 133°. Yield, 25 g.

Questions

1. What difficulty would arise if the sodium acetate were not dried thoroughly?

2. Why is the boiling range of your preparation likely to run low?

3. What side reaction might take place if you heated the flask too strongly at a point where only sodium acetate was present—the acetyl chloride having been driven away too soon?

4. Write an equation showing how you would convert acetic anhydride into an ester.

EXPERIMENT 19

Esters of Acetic Acid

$$CH_3COOH + ROH \rightarrow CH_3COOR + H_2O$$
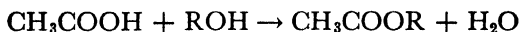
254. When an ordinary carboxylic acid, such as acetic acid, is heated with an alcohol, an ester is formed in a reaction which proceeds to equilibrium. Usually an acid catalyst is required to make this reaction sufficiently rapid to be practical. The reaction is carried out easily with primary alcohols, less readily with secondary, and with great difficulty in the case of tertiary. Since an equilibrium reaction is incomplete, the process is likely to be wasteful unless special technique is introduced. For this purpose the calculation of equilibrium constant K is useful.

$$\frac{Conc_E \times Conc_W}{Conc_{Al} \times Conc_{Ac}} = K,$$

where $Conc_E$, $Conc_W$, etc., represent effective concentrations of ester, water, alcohol, and acid respectively. The catalyst does not appreciably affect this constant if an excessive amount be not used. The following are examples of equilibrium constants of acetic esters obtained by substituting simple experimental values in the above equation.

Methyl	5.24	n-Butyl	4.24	3-Pentanol	2.01
Ethyl	3.96	Allyl	2.18	tert-Butyl	·0.0049
n-Propyl	4.07	iso-Propyl	2.35	Phenol	0.0089

Suppose an equimolal mixture of ethyl alcohol and acetic acid is made. Just before the reaction starts the molal concentration of each reagent may be taken as 1 (per unit volume.) Let x be the molal concentration of ester, and thus of water also, after equilibrium is attained. Then $1 - x$ will be the concentration of residual alcohol and acid, if no volume change has occurred.

$$\frac{Conc_E \times Conc_W}{Conc_{Al} \times Conc_{Ac}} = \frac{x^2}{(1 - x)^2},$$

which must equal 3.96 according to the table above.

216

Then $x = 0.67$, indicating that only about two-thirds of the reagents can possibly be recovered as ester product unless the equilibrium can be displaced.   As observed in § 255, a scheme of continuous distillation is arranged in the interest of better yield.

Where an ester is prepared by mere heating, washing, and distillation of a single quantity of reaction mixture without continuous output, special attention should be directed to the specific constant and to such new technique as may be necessary to ensure adequate yield.

255. Ethyl Acetate.   A 500-cc. distilling flask is fitted with a dropping funnel whose stem reaches almost to the bottom of the vessel.   The arrangement of this detail shown in the illustration of § 234 is appropriate.   The flask is mounted in an oil bath, and is fitted to a water-cooled condenser, with receiver as suggested in Fig. 3, § 33.

Mount a 360° thermometer so that its bulb is in the oil.   Place 20 cc. of 95% ethyl alcohol in the flask, and then add 20 cc. of concentrated sulfuric acid.   Heat the oil bath to 140° and start dropping in through the funnel a solution of 50 cc. of ethyl alcohol in 50 cc. of glacial acetic acid.   Regulate the rate of addition so that the ester is distilled at the rate of about 5 drops per second.   Keep the temperature of the oil as nearly as possible at the 140° mark, letting the regulation of distillation be governed by the dropping funnel.   Continue heating for 5 minutes after the addition is completed.

The distillate contains acetic acid, alcohol, and water as impurities.   To remove the acid, treat the liquid in an open vessel with 2N (or 10%) sodium carbonate solution until the upper layer will no longer redden wet blue litmus paper.   Now discard the aqueous layer, and wash the ester remaining with 10 cc. of water.   Eliminate this portion of wash water carefully, dry the ester layer with anhydrous magnesium sulfate, and distil.   Boiling point of pure ethyl acetate, 77°.   Yield, 20 g.

256. Propyl, Butyl, or Amyl Acetate.   In a 200-cc. round-bottomed flask place 0.5 mole of either propyl, butyl, or amyl alcohol.   Either a normal or iso alcohol is suitable.   To the alcohol add 3 cc. of conc. sulfuric acid, and an amount of glacial acetic acid about 20% in excess of theoretical requirements.   Boil the mixture under a water-cooled reflux condenser, over wire gauze, for 30 minutes.

Transfer the reaction mixture to a distilling flask, and distil until nearly all the liquid has gone over into the flask used as receiver.

Treat the distillate with a concentrated solution of sodium carbonate until the ester layer no longer reddens blue litmus paper. It is best to conduct this neutralization in a large vessel (1 l. or more) on account of the effervescence caused by carbon dioxide.

With the aid of a separatory funnel, separate and discard the aqueous layer. Wash the ester with 25 cc. of water. Dry in a conical flask over about 6 to 8 g. of anhydrous magnesium sulfate. At the next laboratory hour remove the drying agent, and distil the ester.

257. Esters from Acid Derivatives. Acetyl chloride and acetic anhydride are readily converted into their esters by the mere addition, perhaps with gentle heating, of any ordinary primary or secondary alcohol. Such reactions are sometimes too vigorous safely to permit the complete admixture of the reagents all at once. Accordingly, one reagent is placed in a flask under reflux condenser, and the second is slowly added.

After selecting a suitable alcohol, work out the details of the proposed experiment and submit them to the instructor for approval. The following problems should be considered:

1. Apparatus; examine diagrams of §§ 33, 355, and 367 and consider possible combinations which will not permit the escape of offensive vapors into the laboratory.

2. Which of the two reagents should be placed first in the flask?

3. Should the quantity of alcohol equal, exceed, or fall below the value chemically equivalent to the amount of acid derivative used? (See Chap. 4.)

4. Which is the safer procedure, to keep the reagent in the flask cool or · hot while the addition of the other is taking place?

Optional Syntheses

258. Methyl Benzoate. A good example of a readily prepared ester of high boiling point (Refs. 25, 26, 30, 31, 43, 45). **Ethyl benzoate** (Refs. 24, 27, 28, 29, 30, 32, 35, 38) requires somewhat longer time for the esterification reaction.

Methyl salicylate (oil of wintergreen, Refs. 29, 33, 45) and **methyl anthranilate** (Ref. 36), an ester of delightful fragrance much used industrially, require reduced-pressure distillation. The salicylate is somewhat more difficult of preparation than ethyl benzoate, while the anthranilate requires still more skill.

***n*-Butyl-*n*-butyrate.** *n*-Butyl alcohol is simultaneously oxidized and esterified without use of an organic acid provided in advance (Ref. 5).

Questions

1. An equilibrium mixture contained 225 g. of benzyl acetate, 54 g. of benzyl alcohol, 7.2 g. of water, and 30 g. of acetic acid. What is the equilibrium constant for benzyl acetate?

2. What is the greatest possible quantity of phenyl acetate which could be prepared in a simple mixture of 1 mole of phenol and 2 of acetic acid?

3. Explain how continuous distillation (§ 255) affects the yield from an equilibrium reaction.

4. How may yields be improved by use of unequal molal quantities of reagents?

5. If you were required to manufacture *n*-butyl acetate by direct esterification of acid and alcohol, how might you avoid the waste which equilibrium conditions seem to require? (Assume that you are working continuously in a manufacturing plant.)

6. Why is sodium carbonate preferable to sodium hydroxide for removal of acid residues from ester preparations?

7. Outline a laboratory procedure for solving each of the following problems.

(*a*) Is the time of 30 minutes, specified for esterification in § 256, adequate or excessive?

(*b*) Determine the equilibrium constant for esterification of *n*-butyl alcohol and acetic acid.

EXPERIMENT 20

Equivalent Weight of an Ester

259. The equivalent weight of an ester is that weight in grams of the substance from which one equivalent of acid is obtainable by hydrolysis; or that quantity which reacts with one equivalent of alkali. In practice such an equivalent weight is estimated by treating a known weight of the ester with a known quantity of caustic alkali used in excess. The amount of alkali remaining is then readily determined by titration of the reaction mixture with a standard acid solution. The amount of alkali used by the ester is thus revealed, and with it the chemical equivalent of the ester.

Do not interrupt this experiment after the reaction of ester with alkali has been started. If the mixture be allowed to stand until another day, carbon dioxide from the air is likely to enter and react with the residual alkali, thus ruining the determination.

To 150 cc. of 95% ethyl alcohol add approximately 6 cc. (measured in a small graduate) of 50%, carbonate-free potassium hydroxide solution. If potassium hydroxide of suitable purity is not available, substitute 4 cc. of 18N (approximately saturated) sodium hydroxide solution. Sodium carbonate happens to be insoluble in very concentrated sodium hydroxide solutions, and the difficulties encountered with carbonates in alcohol are thus obviously escaped. Place the resulting alcoholic alkali solution in a bottle or flask, stopper securely, and shake well.

Pass a quantity of the alcoholic hydroxide solution through a clean burette and back into the stock bottle; and shake the solution again to ensure mixing with any water which may have been carried down from a newly washed burette. None of the solution is wasted. Now fill the burette to the mark with the alkali solution.

In a very small flask, or a weighing bottle, place a quantity of the unknown ester sufficient for three trials of the experiment. Three grams of material is a suitable amount for an ordinary single substance, 8 g. if it is a true fat (olive oil, tallow, etc.). If the ester is a liquid, place a medicinal eyedropper along with the sample in the flask. If the ester is a low-melting semisolid material, like coconut

oil or butter fat, melt it and treat as an ordinary liquid; but go ahead with the work promptly, before resolidification takes place. The eyedropper permits a neat transfer of the analytical sample without loss by spilling between weighings. If you have not had a course in quantitative analysis, and do not thoroughly understand the significance of the word "quantitatively" in the next paragraph, make the proper inquiries!

Weigh flask, ester, and dropper to 5 mg., using a balance of adequate sensitivity. If the ester is volatile (b. pt. 100° or below), reverse the order of the next two operations (*a*), (*b*), to avoid loss by evaporation.

(*a*) Transfer quantitatively a sample of suitable size (0.8 to 1.2 g., or 30 to 50 drops, of a pure single ester; 2 to 3 g., or 60 to 100 drops, of a true fat) to a 200- to 500-cc. round-bottomed flask, and weigh the flask with dropper again. Do not use samples exceeding the values recommended, or the experiment may be a total failure.

(*b*) Transfer quantitatively about 49 to 50 cc. of the alcoholic alkali solution into the round-bottomed flask mentioned in (*a*).

Boil the mixture of ester and alcoholic alkali under a reflux condenser for 30 minutes or more. Even with high-boiling esters this minimum time allowance will carry the reaction so near to completion that any possible shortage is well within the experimental error of this analytical method.

While the reflux operation takes place, take a clean dry flask to the storeroom to obtain the standard acid, whose normal concentration will be reported to you by the storekeeper. After cleaning the second burette, rinse it with about 5 cc. of the standard acid, allowing the rinsings to drain away as thoroughly as possible. Now fill the burette with a fresh supply of the standard acid. Use this setup to determine the concentration of the alcoholic alkali by titration, with phenolphthalein (5 to 10 drops) as an indicator. The addition of a little distilled water (20 to 30 cc.) to the alcoholic mixture undergoing titration will prevent precipitation of potassium (or sodium) sulfate, and facilitate the process. Record all titration data to the accuracy of 0.05 cc. in the notebook.

At the end of the half hour of refluxing, the reaction mixture of ester and alkali may contain a mass of crystalline salt, nearly insoluble in alcohol. Sodium hydroxide is perhaps more likely to offend in this manner than the potassium reagent. It is barely possible, moreover, that the ester of a di-

basic acid with a short molecular carbon chain, for example diethyl oxalate, $C_2H_5OOC \cdot COOC_2H_5$, might be only half hydrolyzed, precipitating a mixed half-ester-half-salt, of formula such as $C_2H_5OOC \cdot COO^-Na^+$. Should such a compound be left in solid form without further treatment, the analysis would be ruined. To avoid such a situation, proceed as follows. As soon as no further separation of the salt seems to be taking place, add through the reflux condenser just enough distilled water so that the crystals will dissolve at boiling temperature; but do not add more than 50 cc. Now reflux for 15 minutes, and then allow the reaction mixture to cool.

Pour 50 cc. of distilled water through the reflux condenser (or 25 cc. if water has already been added on account of crystallization). Now remove the condenser. Add 5 to 10 drops of phenolphthalein, and titrate the solution with the standard sulfuric acid without removal from the reaction flask.

After the titration is complete, add 2 to 3 cc. of conc. sulfuric acid to the reaction mixture. A volatile substance of characteristic odor may be apparent, or some liquid or solid may separate from the solution. Determine as closely as possible what this material is, noting question 3 below. If the sample is a fat instead of a single substance of definite composition, calculate its **saponification number**—that is, the number of milligrams of potassium hydroxide required to react with 1 g. of the fat. The resulting value may be compared with known values given in the Appendix (§449). In view of the international custom in reporting milligrams of potassium hydroxide, report values in such terms, even though sodium hydroxide may actually have been used.

Calculations. Make the necessary calculations to show what quantity of alkali was removed by reaction with the ester. From this value calculate the equivalent weight of the ester. If the value so reported does not agree with the character of the sample analyzed, repeat the determination. There should be enough alcoholic standard solution left for one repetition, if care has been taken.

In making the written laboratory report of this determination, arrange data in tabular form and, after entering the calculations suggested above, show comparison with the theoretical value calculated from the formula of the ester.

By use of diethylene glycol as a solvent instead of alcohol, the determination may be expedited. [Redemann and Lucas, *Ind. Eng. Chem. Anal. Ed.* **9,** 521 (1937).]

Questions

1. What is the chemical composition of the mixture just after the reflux operation, but before titration?

2. What is the chemical composition just after titration?

3. What is the composition after the excess of sulfuric acid is added at the end of the experiment?

4. Calculate the equivalent weight of (*a*) methyl formate, (*b*) ethylene glycol oxalate, (*c*) ethyl acid phthalate, (*d*) ethyl succinate.

5. Why is an oversize weighed sample of ester undesirable in this experiment?

6. Why do we weigh out a specially large sample when a fat is being tested?

7. Could methyl orange be used satisfactorily in this experiment?

8. Glycol ($C_2H_6O_2$) is said to contain two alcoholic hydroxyl groups per molecule. How might you use the above experiment as part of a method of proving that fact?

9. Which substance would have the higher saponification number, glyceryl tributyrate or glyceryl tristearate? Why?

EXPERIMENT 21

Hydrolysis of an Ester and the Identification of the Acid Constituent

260. In this assignment either a known or an "unknown" ester is analyzed, according to notice given by the instructor. Esters chosen for the experiment are restricted to (*a*) those which yield crystalline acids of **low solubility,** and (*b*) those belonging to the lower range of simple monobasic fatty acids, which are **volatile.**

Place 40 cc. of 6N sodium hydroxide and 10 cc. of the ester in a 200-cc. round-bottomed flask. Attach a water-cooled reflux condenser and heat the mixture to boiling. If the ester has not dissolved to a considerable extent in the aqueous hydroxide, cool the mixture slightly and add 30 cc. of ethyl alcohol. Boil the final mixture gently for one-half to one hour.

Remove a 1-cc. sample, and acidify it with dilute hydrochloric acid. Under the specified conditions of the experiment, either of two results should be obtained: (*a*) an immediate precipitate of a solid acid, usually of the aromatic series, in which case proceed as in § 261; or (*b*) a clear solution, inferring the alternative of a volatile aliphatic acid, in which case proceed as in § 262.

261. Solid Acid. Filter the reaction mixture if necessary to remove solid impurities. Acidify the filtrate with hydrochloric acid, and continue to add acid until a sample of the filtered solution yields no more crystalline organic product upon further acidification. Not more than 25 cc. of conc. hydrochloric acid are required. Cool the mixture, collect the product on a Buechner filter, and recrystallize from boiling water, noting suggestions of §§ 95 and 100.

After the crystals are dry, determine their melting point as described in §§ 203 *ff.*, and find the equivalent weight by titrating two or more 1-g. samples with standard alkali solution of about N/2 concentration. For details of such an experiment, see a similar assignment given by Bray and Latimer (*Course in General Chemistry,*

Macmillan). If the experiment dealt with an unknown ester, report information to the instructor and draw whatever conclusions are possible.

Questions

1. Why is alcohol used in this experiment?

2. What is the chemical composition of the mixture just before the hydrochloric acid is added?

3. What is the chemical principle governing the action of hydrochloric acid in this experiment?

4. Would sulfuric acid be satisfactory here in place of hydrochloric acid? (Consider both theoretical and practical laboratory conditions.)

5. Suppose you had desired to prepare acetic acid (from ethyl acetate) instead of benzoic acid. In what way would you change the procedure? Why?

6. Suppose methyl oxalate were issued as an "unknown" in this experiment. What practical difficulties might arise?

262. Volatile Acid—Duclaux Analysis. In this procedure the volatile acid is freed from all accompanying substances except water, and in the process is finally obtained as a dilute solution whose concentration is of the order of 2%. This dilute solution is then distilled into certain arbitrary fractions. Analysis of these fractions (by titration) gives the Duclaux numbers. Read §§ 71 and 72 before proceeding with the experiment.

Distil the alkaline reaction mixture until about 35 cc. (mostly alcohol, if any) has been expelled. To the residue in the distilling flask add 2 drops of phenolphthalein and neutralize with 3N sulfuric acid; then add 10 cc. more of the acid. During this process the flask should be cooled in tap water. Distil the resulting solution into a new receiver until the volume of the residue in the distilling flask has been reduced to 20 cc. Dilute the distillate to a final volume of 250 cc., and mix thoroughly.

By titration find how many cubic centimeters of a given sodium hydroxide solution are required to neutralize 10.00 cc., quantitatively measured, of the diluted distillate just prepared. For this purpose a sodium hydroxide solution of about 0.1N concentration is suitable; it need not be standardized, but an adequate supply must be available for the titrations to follow.

Place 100 cc. of the diluted distillate, which is actually a dilute

solution of the acid under investigation, in a distilling flask and distil three 10-cc. portions at a constant rate, collecting each portion in a 10-cc. graduated cylinder. Titrate each 10-cc. portion with the sodium hydroxide used above. Calculate the percentage of the total acid which came over in each of the three portions, and compare with the Duclaux constants given in § 72.

Questions

1. What logical relation might the differences in molecular structure of the acids have to the respective differences in Duclaux constants?

2. Make a reasonable prediction of the magnitude of the Duclaux constants in the series of acids above caproic, as the carbon chains become successively longer.

3. How do you explain the fact that the second and third Duclaux constants of acetic acid are larger than the first, whereas the second and third of butyric acid are smaller?

4. How might the Duclaux method be used to determine the ratio of acetic and propionic acids in a mixture of the two?

5. Show how the Duclaux constants of propionic acid prove that this acid and water necessarily form an azeotropic mixture of minimum boiling point.

6. The azeotropic mixture of n-butyric acid and water contains more than 2% of butyric acid. Assuming that the table of Duclaux constants (§ 72) applies to 2% solutions, show how the above statement about n-butyric acid could be predicted from the tabular values.

7. How could the Duclaux method be used to find the azeotropic composition of propionic or butyric acid?

EXPERIMENT 22

Fats and Soaps

$$C_3H_5(OOC\ R)_3 + 3KOH \rightarrow C_3H_5(OH)_3 + 3R\ COOK$$
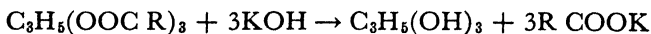
263. Inasmuch as all ordinary fats, including vegetable oils, are the glyceryl esters of fatty acids, a mixture of the potassium salts of these acids may readily be prepared by alkaline hydrolysis of a fat. The experiment is identical in principle with that of § 259. The carbon chains in these potassium salts are mostly fairly long (6 to 20 or more carbon atoms), and the salts have special colloidal properties resulting in their usefulness as soaps.

In a 200-cc. round-bottomed flask fitted with a water-cooled reflux condenser, heat a mixture of 5 g. of solid potassium hydroxide, 75 cc. of alcohol, and 5 g. of an animal or vegetable fat (or oil). Different students may well select different types of fat:

(*a*) Suet, tallow, or lard.

(*b*) Butter fat (butter which has been melted and freed from water and salt).

(*c*) Vegetable oil—cotton, corn, olive, rape-seed, sesame.

(*d*) Coconut oil.

(*e*) Drying oil—linseed, fish, poppy seed.

(*f*) Hard-hydrogenated vegetable oil (see § 23).

When the reaction is complete (in not more than 30 minutes), no globules of oil are obtainable when a test sample of a few drops is mixed with water.

Distil the reaction mixture, recovering the alcohol, and dissolve the residue in about 50 to 75 cc. of distilled water.

264. Reactions of a Soap. (*a*) To a 10-cc. sample of the solution add a few drops of calcium chloride solution and shake. Now add a quantity of trisodium phosphate approximately equal to the calcium chloride and shake again. Changes in foaming characteristics are significant here.

(*b*) Acidify a second portion with dilute sulfuric acid, and note the characteristics of the resulting precipitate both at room temperature

227

and at 80° or above.   The choice of a particular type of fat is particularly significant in this test.   Notice odor, if present.

(c) Acidify the rest of the solution with dilute sulfuric acid, and separate the insoluble organic product.   Dissolve this in a few cubic centimeters of carbon tetrachloride, and add a few drops of a solution of bromine in carbon tetrachloride.   Compare with results from the saponification of some other fat.

265. Glycerol.   The filtrate from experiment (c) contains glycerol, which may be obtained by exactly neutralizing the mixture with sodium carbonate, evaporating to dryness and extracting with absolute alcohol.   Evaporation of the alcoholic extract yields glycerol.

266. Sulfate and Sulfonate Soaps.   Dissolve about 1 g. of one of the synthetic "wetting-agent" soaps in about 50 cc. of water, and shake a small sample in a test tube.   Test the material with calcium chloride in the same manner employed in § 264 with ordinary soap, and compare results.

Optional Experiment

267. Myristic Acid ($C_{13}H_{27}COOH$) exists in the form of its glyceryl ester as the main constituent of nutmeg oil.   The ester and the free acid are thus obtainable by a process similar in principle to that of § 263 above, illustrating the comparatively rare case where a single fatty acid is obtained directly from its simple natural glyceride (Ref. 6).

Questions

1. Explain the primitive process of boiling slaughterhouse fat residues with water which has passed through wood ashes.

2. What everyday situation corresponds to the above experiment with calcium chloride?   With trisodium phosphate?

3. Explain why soap might be expected to be useful in cleaning.

4. Soiled clothes are often contaminated with acidic substances.   Why does this fact concern the laundry operator?

5. Why should butter require more careful handling in storage than olive oil, to be acceptable as food?

6. Devise a laboratory method of distinguishing genuine butter from an imitation made of lard and hydrogenated cottonseed oil.

7. Why is linseed oil superior to corn oil for use in paints?

EXPERIMENT 23

Aliphatic Amides

$$CH_3COONH_4 \rightarrow CH_3CONH_2 + H_2O$$

268. Simple heating of the ammonium salt of an organic acid frequently causes the substance to be converted into the corresponding amide. Since these ammonium salts are relatively uncommon in trade, they are expensive. It is thus more economical to prepare an ammonium salt at the outset of the amide experiment.

269. Acetamide. Cautiously mix 0.4 mole of ammonium carbonate (monohydrate) and 1.5 mole of glacial acetic acid in a 200-cc. round-bottomed flask and heat under a water-cooled reflux condenser for an hour or more. After this period replace the condenser with a small fractionating column carrying a thermometer. Place the condenser in position for distillation, and distil very slowly, so that the temperature at the top of the column does not exceed 105°. It will probably take more than an hour to reach the point where no further distillate can be obtained at temperatures near 100°. (If the distillation be conducted rapidly, a low yield of amide will result.) When it is no longer possible to continue distillation at temperatures specified above, heat the flask more strongly and expel as much as possible of the excess acetic acid. The temperature may now rise to 120° or more.

After the low-boiling components have been eliminated as completely as is possible with a column in the line, stop the distillation and cool the residue in the flask. Transfer this residue to a small distilling flask with side stem connected to an adapter or to a short air-cooled condenser.

The mixture consists largely of acetamide dissolved in acetic acid. Despite the wide spread between the boiling points of the components (over 100°) it is not as easy to separate the substances as the temperature difference suggests. Fractionation is necessary. Read § 73 before conducting this part of the experiment.

Slowly distil two fractions into small flasks; the first from the initial boiling point to 195°; the second from 195° until the end. After the second fraction has become cool it should yield a quantity of crystalline acetamide, which is collected on a suction filter. Preserve the filtrate and add it to fraction No. 1. A refractionation of the liquid product will afford an additional yield of acetamide.

The combined crystalline product is pressed between sheets of filter paper, and weighed without further attempt to dry. Yield, 25 g. (If a higher degree of purity of acetamide is desired, the crystals may be washed with a 10% solution of alcohol in ether, and then with a little ether; or they may be recrystallized from chloroform or benzene.) Melting point of pure acetamide, 81°.

270. Urea. This compound may be prepared either from its natural source, the urine, or by the famous Liebig-Wöhler synthesis from ammonium cyanate. This compound has the unique characteristic of two NH_2 groups in amide linkage with but one carboxylic acid group, a feature naturally possible only in the case of carbonic acid. This excess of amine renders urea distinctly basic.

271. Reactions of Urea. (*a*) Dissolve a few minute crystals of urea in a drop of water on a microscope slide. Touch this solution with a stirring rod which has been dipped in conc. nitric acid. Crystals of urea nitrate separate. Cover with cover glass, remove excess liquid with filter paper, and examine crystals under low-power microscope, taking care not to allow acid solution to get on metal of the instrument.

(*b*) If no microscope is available, dissolve 1 g. of urea in 15 cc. of water and add 4 cc. of conc. nitric acid. Upon cooling, crystals of urea nitrate separate.

(*c*) Place 2 cc. of dilute sodium hydroxide in each of two test tubes. To one add a few crystals of ammonium carbonate, to the other a like quantity of urea. Note the odor of each tube. Now warm each mixture gently, and again compare odors. On a basis of this evidence, how might salts and amides be distinguished?

Dissolve about 0.5 g. of urea in 3 cc. of water, and mix this with an alkaline solution of sodium hypobromite, prepared by mixing 5 cc. of bromine water with 5 cc. of dilute sodium hydroxide solution. How might the resulting reaction, yielding gaseous nitrogen, be used as the basis of a method of quantitative analysis for urea?

Cautiously heat about 0.5 g. of urea in a dry test tube until the melted mass becomes opaque and solid. This product contains the substance **biuret.** Its presence is indicated by the characteristic color exhibited when the material is treated with 5 cc. of dilute sodium hydroxide and a few drops of very dilute cupric sulfate solution.

Optional Syntheses

272. Acetamide. This compound may be made directly from ethyl acetate, as illustrated in Refs. 24, 26, 31, 39.

Benzamide. Illustrating the use of an acid chloride and ammonia (Refs. 25, 27, 28, 29, 30, 32, 34, 35, 38, 39, 40, 43, 45).

Urea. (Refs. 23, 28, 30, 31, 32, 35, 39, 40, 41.)

Questions on Acetamide

1. What is the chemistry of the first reaction in this experiment?

2. Why is the first distillation conducted so slowly?

3. What is the relation of the speed of distillation to chemical equilibrium in this process?

4. How could you transform the product into acetic acid again? Into methylamine?

5. Why do we use ammonium carbonate instead of the cheaper ammonium hydroxide?

6. Acetamide has been advertised commercially as a peculiarly effective "universal" solvent. Why would one expect the substance to have the ability of dissolving a great variety of organic compounds?

CARBOHYDRATES

Experiments 24–29

EXPERIMENT 24

Reactions of Sugars

273. The first experiments are directed principally to the following main features of chemical structure.

(*a*) Presence of an aldehyde or α-hydroxyketone group in the molecule, which is revealed in some reactions by (1) reactivity as a reducing agent, and in others by (2) the ability to combine with an auxiliary reagent to form a crystalline aldehyde or ketone derivative.

(*b*) Presence of alcoholic groups, which react to form esters of practical value.

(*c*) Presence of oxygen-bridge or oxygen-ring linkages, particularly in di- or poly-saccharides, which prevent certain reactions otherwise normally expected of a carbohydrate.

274. Aldehyde Reactions. Prepare a solution of 1 g. of glucose in 10 cc. of water, and provide for comparison about 10 cc. of 5% formaldehyde solution.

(*a*) *Silver Mirror Test.* Prepare ammoniacal silver nitrate reagent as described in § 237, and add to 10-cc. portions of this reagent, in specially cleansed test tubes, (1) a few drops of the formaldehyde solution, (2) 2 cc. of glucose solution. Note experimental details of § 237, including the necessity of prompt disposal of any of the silver reagent which may be left over.

(*b*) *Fehling's Solution.* Prepare 10 cc. of this reagent just before use, by mixing 5 cc. of "No. 1" (a 3% solution of cupric sulfate cryst.) and 5 cc. of "No. 2" (a 15% solution of Rochelle salt in 5% aqueous sodium hydroxide). The resulting mixture should be dark blue and clear.

Heat 5 cc. of the mixed solution to boiling, and gradually add glucose solution drop by drop. Cuprous oxide is precipitated. Repeat with formaldehyde. (If too much formaldehyde is used, the reduction may proceed even to the stage of metallic copper.)

(c) *Schiff's Reagent.* Test glucose and formaldehyde solutions by addition of 1 cc. of Schiff's reagent to each. This is a direct test for *free* aldehyde groups.

(d) *Osazone Formation.* Sugars containing aldehyde or α-hydroxyketone groups react with phenylhydrazine, yielding osazones, in which two molecular residues of the hydrazine have united with one of the sugar. Sugars may be identified by the length of time required to form the yellow crystalline products as well as by conventional melting-point methods.

The times for osazone formation are listed below for several sugars. Perform the following experiment with glucose. If the reaction time agrees with that listed for glucose, repeat the experiment with another sugar. This second sugar will be one from the list given below. It may be either a known compound, or an "unknown" issued individually to the student, according to notice given by the instructor.

Place 0.20 g. of glucose in a test tube with 0.40 g. of phenylhydrazine hydrochloride, 0.60 g. of sodium acetate, and 4 cc. of distilled water. (Weigh these materials on a balance accurate to 0.02 g. or less.) Stopper the test tube with cotton and place it in a beaker of boiling water. Note the time of immersion and the time when precipitation of the osazone first occurs. Shake the tube occasionally to prevent supersaturation.

(*Optional.* A more elegant and trustworthy method of handling this problem would include recrystallization of the osazone and the determination of its melting point. The product may also be compared with known osazones with the aid of a low-powered microscope.)

APPROXIMATE TIMES OF OSAZONE FORMATION, MINUTES

Mannose	0.5
d-Fructose	2
d-Glucose	4 to 5
l-Xylose	7
l-Arabinose	10
d-Galactose	10 to 18
(Sucrose)	30

Note that the product from mannose is the simple hydrazone, and that from sucrose is merely the one obtained from the products of hydrolysis of the disaccharide. Possible confusion of the osazones from arabinose and galactose may be avoided by noting that the first is an oily product as commonly prepared, whereas that from galactose is crystalline in nature.

EXPERIMENT 25

Mucic Acid from Lactose

275. Vigorous oxidation of a sugar may produce carboxyl groups at both ends of the monosaccharide carbon chain. In this experiment a disaccharide first splits into two portions, each of which is oxidized to a six-carbon dibasic acid.

Place 15 cc. of water in a 5-inch evaporating dish in order to be able to make an approximate estimate later showing when the reaction mixture shall have been evaporated down to that volume. Now add 40 cc. more of water, 22 cc. of conc. nitric acid, and 7 g. of lactose. Evaporate the resulting solution outdoors, in a hood, or with other means of disposal of acid fumes, until the volume is reduced to 15 cc. Cool the mixture, dilute with 25 cc. of water, and collect the crystalline product on a suction filter.

The crude mucic acid may be recrystallized by carefully dissolving it in the minimum quantity of dilute sodium hydroxide and reprecipitating with hydrochloric acid at temperatures not exceeding 25°. Yield, 2.5 g. Melting point (with decomposition) of mucic acid, 206°.

EXPERIMENT 26

β-*d*-Glucose Pentacetate

276. This experiment illustrates a method of identifying sugars. A compound with several highly polar(hydroxyl) groups in the molecule, such as a sugar, is likely to have unsatisfactory melting behavior. Conversion into an ester brings the material into lower and more convenient melting-point range. The procedure described below should not be interrupted until the reaction mixture is poured over ice and the solid product crushed.

In a dry porcelain mortar grind together 5 g. of dry glucose and 4 g. of anhydrous sodium acetate, and place the powdered mass in a 200-cc. round-bottomed flask. Add 25 cc. of acetic anhydride and heat on the steam bath under air-cooled reflux condenser until the solids are dissolved (about 30 minutes). Now continue heating for 2 hours more, and pour the reaction mixture into about 300 cc. of ice water containing a few pieces of crushed ice. Break up the resulting solid product and allow the finely divided suspension to stand for at least 2 hours, or until the next laboratory period.

Collect the solid product on the Buechner filter, wash with a little cold water, and press down until as nearly water-free as possible. Recrystallize from ethyl alcohol (about 20 to 25 cc.). Yield, 6 to 7 g. Melting point of pure β-*d*-glucose pentacetate, 132°.
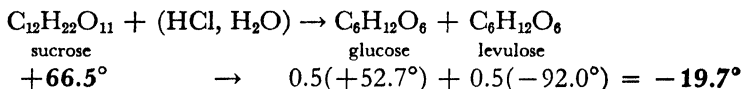
Questions

1. What relation does the designation "β" in the name of this product have to the question as to which five of the six carbon atoms in glucose are acetylated?

2. How could you use your final product in a laboratory experiment to prove that just five acetyl groups had combined with the glucose nucleus?

EXPERIMENT 27

Inversion of Sucrose

277. When sucrose is hydrolyzed, equal quantities of the monosaccharides glucose and levulose are produced. These sugars differ materially from the parent disaccharide not only in strictly chemical reactions (§ 278) but also in optical rotation (§ 279). It happens that levulose is strongly levorotatory. The conversion of dextrorotatory sucrose into a mixture which is half levulose thus causes the optical rotation to shift, or "invert," from a dextro value to a levo or left angular reading. If only part of the original sugar sample was sucrose, the rotation may not become levo, but instead may shift a short angular distance to a lower dextro reading. Evidence is thus obtained of the fraction of sucrose in the mixture.

The specific rotations of the three sugars are, sucrose $+66.5°$, glucose $+52.7°$, and levulose $-92.0°$. For simplicity in explanation, suppose a solution containing 1 g. of sucrose per cubic centimeter of solution (standard reference concentration) were heated with 5% of its volume of conc. hydrochloric acid, and thus became completely hydrolyzed. The reaction mixture would contain approximately 0.5 g. of glucose and 0.5 g. of levulose per cubic centimeter of solution. The change in rotation is represented by simple arithmetic.

$$C_{12}H_{22}O_{11} + (HCl, H_2O) \rightarrow C_6H_{12}O_6 + C_6H_{12}O_6$$

sucrose · glucose · levulose

$$+66.5° \rightarrow 0.5(+52.7°) + 0.5(-92.0°) = -19.7°$$

Since the standard reference concentration of 1 g. per cubic centimeter is too high for practical work with a polarimeter, more dilute solutions are used in § 279, involving simple proportionate reductions in numerical values.

For the following experiment it is necessary to have sucrose which has not been exposed to the acid fumes of a laboratory or storeroom; preferably cane or beet sugar fresh from grocery stock.

278. Chemical Reactions. Prepare a stock solution of 4 g. of sucrose in 40 cc. of water. To 25 cc. of this solution in a test tube or

small flask add 1 cc. of conc. hydrochloric acid, and heat for 5 to 10 minutes in a hot water bath (70° to 90°). Cool the reaction mixture to room temperature. Preserve the remainder of the sugar solution free from acid.

Test small portions (2 or 3 cc.) of each of these sugar solutions with each of the following reagents according to methods already described in § 274. Explain differences or likenesses in reaction in each case.

Ammoniacal silver reagent.

Fehling's solution.

Schiff's reagent.

To a 10-cc. portion of the acid-catalyzed sugar solution in a large test tube add 2 cc. of phenylhydrazine (keep off from the skin) or 2.5 g. of phenylhydrazine hydrochloride and 3 g. of sodium acetate. Treat with ammonium hydroxide until the solution is neutral to litmus, and stand the test tube in a beaker of boiling water. No further heating of the beaker is required after this operation. After a half hour or more cool the solution and collect the osazone product on a suction filter.

Recrystallize as much of the osazone as may be convenient from 40 to 50 cc. of 70% aqueous ethyl alcohol. Use a flask under reflux condenser, as described in § 101. Cool the solution, filter, dry the crystalline product, and examine under a low-powered microscope.

279. Optical Rotation. Obtain one of the following solutions, as designated by the instructor:

(*a*) A solution of known concentration made by dissolving about 10 g. (accurately weighed) of sucrose in about 40 cc. of water and diluting to just 50.0 cc.

(*b*) A solution of pure sucrose of unknown concentration, furnished by the instructor; concentration to be determined.

(*c*) A sirup containing not only sucrose, but an uncertain quantity of monosaccharides such as glucose and levulose.

Using a polarimeter, determine the rotation of the solution before any chemical reaction is attempted, carefully preserving the entire solution for the next operation. Now treat the whole solution with 2.5 cc. of pure conc. hydrochloric acid, place in a conical flask and heat in a water bath to 65° to 70° for 15 minutes. Allow the mixture to stand for an additional 15 minutes without attempt to heat or cool. Finally cool to room temperature, place in the polarimeter

tube, and determine the rotation. The following calculations are then appropriate, according to the experiment chosen.

(*a*) Determine the specific rotation of sucrose.

(*b*) Prove arithmetically that the unknown solution contains no appreciable quantity of glucose.

(*c*) Determine the percentage of sucrose in the solution, basing your calculation on the amount of inversion of polarimetric reading observed.

280. Hydrolysis of Starch. Grind about 1 g. of starch with 10 cc. of cold water, pour the milky suspension into 200 cc. of boiling water, and set aside to cool. Part of the material will pass into a pseudo solution which is colloidal in nature. Pour out about 5 cc. of this solution and test with a very dilute solution of iodine in potassium iodide.

Now add 10 cc. of conc. hydrochloric acid to the remainder of the starch solution, and heat the mixture to boiling. Every 5 minutes pour out 5 cc. of the boiling solution, cool the sample, divide into two equal portions, and apply the iodine and Fehling's tests, respectively. Discontinue the periodic tests when no further change in results is noted.

281. Cellulose—Schweitzer's Reagent. To 5 cc. of Schweitzer's reagent (2% solution of cupric hydroxide in conc. ammonium hydroxide) add a piece of filter paper about the size of a 25-cent piece. Pour the resulting solution into dilute hydrochloric acid.

EXPERIMENT 28

Cellulose Nitrate

282. In a 250-cc. beaker place 20 cc. of conc. nitric acid (sp. g. 1.42) and add 20 cc. of conc. sulfuric acid. While this solution is still warm, add 0.5 g. of absorbent cotton. Stir the mixture for just 3 minutes. Remove the cotton with a glass rod, freeing it as much as possible from acid, and immediately wash it with a large quantity of cold water. Squeeze the cellulose nitrate product as dry as possible and allow to dry in the open air. *Do not heat the material.*

Test the inflammability of the dry cellulose nitrate by placing a small fragment on a brick or stone, and lighting with a burner, not a match; or use tongs.

Cellulose nitrate prepared in this way contains mostly lower nitrates rather than the more dangerous guncotton, or trinitrate. Test the solubility of the nitrate ester in a mixture of 5 cc. of ether and 5 cc. of ethyl alcohol. Pour a few drops of the resulting solution (collodion) into water. Allow the remainder to evaporate on a watch glass or evaporating dish. Finally destroy all residues of cellulose nitrate before you leave the laboratory.

EXPERIMENT 29

Cellulose Acetate

283. In a small conical flask place 0.5 g. of absorbent cotton, 20 cc. of glacial acetic acid, 6 cc. of acetic anhydride, and 2 drops of concentrated sulfuric acid. Stir with a glass stirring rod until the cotton is well distributed through the mass of the solution, and all air bubbles have been eliminated. Stopper the flask and let stand for 12 hours or more. With stirring, pour the reaction mixture in a thin stream into 0.5 l. of water. The cellulose ester should separate out in solid form; collect it on a Buechner filter, wash with water, and press the mass between filter papers or upon a porous plate until dry.

Dissolve half of the cellulose acetate in 20 cc. of chloroform contained in a small beaker or test tube. It may require some time for the material to pass into solution. If the solution is turbid, probably water is present, in which case it should be dried with the aid of a small amount of calcium chloride in the usual way. Pour the dry solution upon a watch glass (out of doors) and let it evaporate slowly. When the chloroform has disappeared, add water, which helps to loosen the cellulose acetate film from the glass. Remove the product and test its inflammability.

Optional Experiments

284. Isolation of Individual Sugars from Natural Sources. Lactose from milk, glucose from sucrose, etc., described in several manuals. (For examples, Refs. 27, 30, 32, 36, 39, 40.)

Questions

1. How do we explain the fact that glucose resists the action of Schiff's reagent?

2. In the light of question 1, how do you explain the other aldehyde reactions?

3. Show by structural formulas how levulose may be converted into the *same* osazone as glucose.

4. Write an equation for the transformation of lactose into mucic acid.

5. In what way are cellulose and starch related to the simple sugars?

6. Explain why sucrose and starch will react with Fehling's solution after hydrolysis but not before.

7. A certain solution of cane sugar, adulterated with glucose, had a rotation of $+20°$. After boiling with hydrochloric acid, the rotation was $+5°$. What fraction of the sugar in the original solution was glucose?

EXPERIMENT 30

Nitrobenzene

$$C_6H_6 + HNO_3 \rightarrow C_6H_5NO_2 + H_2O$$
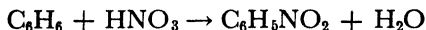
285. Nitration. By contrast with its behavior in inorganic chemistry, nitric acid releases a hydroxyl group instead of a hydrogen atom in reacting with an aromatic hydrocarbon or appropriate aromatic derivative. The organic compound yields the necessary hydrogen to form water, and is converted into a nitro derivative. The addition of concentrated sulfuric acid causes this reaction to proceed more effectively, particularly at desirable lower temperatures and during the latter portion of the reaction period when accumulated water is retarding the process.

Oxides of nitrogen, either present in the nitric acid reagent, or formed in a side reaction during nitration, may well be eliminated. A small amount of urea destroys nitrous acid present and thus eliminates the oxides of nitrogen, equivalent of nitrous acid.

Caution. *Nitrobenzene is distinctly toxic and its vapor should not be allowed to escape into the atmosphere of the laboratory. See that the delivery tube of the condenser passes well into the mouth of the flask receiver. It is not permissible to allow distillates of liquids in the aromatic series to drip through the open air into beakers or bottles. This applies to aniline, toluidine, and other substances described in the following pages, as well as nitrobenzene.*

To 30 cc. of conc. nitric acid (s.g. 1.42) in a flask add slowly 30 cc. of conc. sulfuric acid, and cool the mixture in running water. Place 0.4 mole of benzene and 1 g. of urea in a 500-cc. flask, and provide a thermometer (110° range). In view of the shaking required in the process, it is convenient to hold the thermometer in the flask with the aid of an old cork which has been channeled in such a way as to permit the addition of liquid. Now add slowly in small portions the acid mixture above prepared. From time to time cool the flask in running water so that the temperature of the reacting mixture ranges from 45° to 50°. *Frequent* and *vigorous* agitation is necessary to permit the acids and the benzene to come into contact with each

other and react; otherwise they lie in two layers, one of which may become unduly warmer than the other. After all of the acid has been added to the benzene, hold the reaction mixture, with occasional shaking, at the temperature of 60° for 30 to 40 minutes. A hot water bath and running water should be at hand for use according to the demands of the situation.

Cool the reaction mixture, then separate and discard the acid layer. Wash the nitrobenzene layer first with 60 cc. of water, and then with a mixture of 5 cc. of the laboratory solution of sodium carbonate and 25 cc. of water. If the mixture, after thorough shaking, is acid to litmus, repeat the sodium carbonate treatment until a neutral or alkaline test is obtained. Finally wash with 50 cc. of water.

The washed product is likely to contain emulsified water. Remove this by heating gently with anhydrous calcium chloride (about 12 g.) for a few moments, then cooling the mixture, with shaking, to room temperature. Allow the product to stand with the calcium chloride until it is dry, preferably for several hours or days.

Separate the dry nitrobenzene from the calcium chloride, transfer to a small distilling flask, and distil through an air-cooled condenser. Collect the distillate coming over between 200° and 208° (uncor.), and reject the high-boiling residue. Do not attempt to distil a higher boiling fraction, lest there be a violent decomposition of higher nitro compounds present. If any large residue is left, it is likely that the reaction was allowed to take place at too high a temperature, particularly at first when the acids were at maximum concentration. The product should not smell of nitric acid. Yield, 30 g.

Optional Syntheses

286. m-Dinitrobenzene. Nitrobenzene is heated with fuming nitric acid, or a mixture of solid sodium nitrate and concentrated sulfuric acid, yielding the solid dinitro derivative (Refs. 24, 26, 27, 28, 29, 30, 34, 35, 37, 39, 40, 43, 45).

p-Bromonitrobenzene. Nitration of bromobenzene (Ref. 23).

o- and p-Nitrophenol. Nitration of the highly reactive phenol with dilute nitric acid is readily accomplished. The experiment also illustrates separation of ortho and para isomers by steam distillation (Refs. 27, 28, 30, 32, 34, 35, 38, 39, 41, 43, 45).

o- and *p-*Nitrodiphenyl. This experiment also illustrates the separation of isomers (Ref. 29).

Trinitro compounds. *sym-*Trinitrophenol, picric acid (Refs. 27, 30, 32, 38, 43, 45). *sym-*Trinitrotoluene, "TNT." See *J. Chem. Soc. Abstracts,* **64,** 14 (1893).

Questions

1. Why is the acid added gradually to the benzene, instead of benzene to acid?

2. Why should one be more particular to avoid a high temperature at the start of the reaction than toward the close?

3. Is the correction for exposed stem of the thermometer of great significance here? Why?

4. Suppose (*a*) chlorobenzene, (*b*) benzoic acid, were nitrated instead of benzene. What products would you expect?

EXPERIMENT 31

2,4-Dinitrotoluene

287. 2,4-Dinitrotoluene. The introduction of a second nitro group into the nucleus of a mono-nitro derivative of benzene is usually more difficult than the first nitration. The more active fuming nitric acid (see § 447) is therefore convenient. In this case, however, ordinary concentrated nitric acid may be used, if the quantity of nitric and sulfuric acids is increased about 40%.

Caution. Be very careful to keep fuming nitric acid off the skin, as it reacts vigorously and causes stains and serious burns.

In a 250- or 300-cc. flask place 18 g. of fuming nitric acid and 30 g. of conc. sulfuric acid. To these is added gradually in small portions 14 g. of *p*-nitrotoluene. After the addition of each portion cool the reaction mixture by immersing the body of the flask in cold water. After all of the *p*-nitrotoluene has been added, place a small funnel in the mouth of the flask, stem down. In this way undue diffusion of vapors from the flask is discouraged; at the same time the small hole in the stem gives adequate opportunity for release of pressure if any.

Heat the flask and contents in a water bath at about 90° or 95° for 30 minutes, and then cool nearly to room temperature. Now pour the reaction mixture in a fine stream into about 800 cc. of ice water containing a few pieces of ice. The solid which separates is crude 2,4-dinitrotoluene. Collect the product upon the Buechner filter, wash well with cold water, and recrystallize from hot methyl alcohol. Yield, 12 g. (*Caution.* Fire hazard in recrystallization with volatile methyl alcohol, boiling pt. 65°. See § 101.) Pure 2,4-dinitrotoluene melts at 70.7°.

Questions

1. Why is it better to use *p*-nitrotoluene in this experiment than the cheaper isomer *o*-nitrotoluene?

2. Why not put in both nitro groups at one time, starting with toluene and using fuming nitric acid?

288. 2,4-Dinitrophenylacetic Acid (Compound used in § 393). In a 200- or 300-cc. flask place 0.5 mole of fuming nitric acid (note § 447), add 50 cc. of conc. sulfuric acid, and insert a thermometer into the mixture. Now add in small portions, with shaking, 0.1 mole of phenylacetic acid, which should not be pulverized. The rate of addition may be as high as possible provided the temperature of the reaction mixture is kept between 60° and 65°, frequent use being made of an ice bath. At the close of the nitration allow the temperature to mount to 70°, and set the flask aside on the desk for 10 minutes. Now pour the reaction mixture (without previous cooling) upon a mixture of about 200 g. of ice and 100 cc. of water in a beaker. Collect the precipitate of crude 2,4-dinitrophenylacetic acid on a Buechner filter, wash it with a little ice water, and re-crystallize from 650 cc. of water, which has been brought to a boil *before* addition of the organic preparation. (*Note.* This compound should not be heated to temperatures over 80° for any longer than necessary.) It does not have a sharp melting point.

This product may also be recrystallized from glacial acetic acid, in which it is much more soluble at boiling temperature.

EXPERIMENT 32

p-Nitrobenzoic Acid

$$\text{NO}_2 \quad \text{oxidized} \rightarrow \quad \text{NO}_2$$
$$\text{CH}_3 \qquad\qquad\qquad \text{COOH}$$
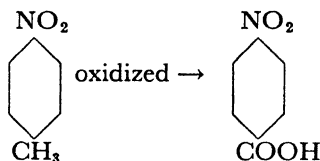
289. Direct oxidation of the methyl group in the molecule of toluene to yield a carboxyl group is difficult in the laboratory. When certain substituent groups are present upon the toluene ring, however, direct oxidation is readily accomplished. In the illustration described below, dichromate ion in the presence of a strong acid is a suitable oxidizing agent for the preparation of *p*-nitrobenzoic acid.

In a 500-cc. round-bottomed flask place 0.1 mole of *p*-nitrotoluene, 48 g. of sodium dichromate (dihydrate), and 60 cc. of water, and attach a water-cooled reflux condenser. The outfit illustrated in § 355 may be used to advantage. (See also § 24.) Now pour 70 cc. of concentrated sulfuric acid into 35 cc. of water contained in a beaker or flask. Cool the vessel sufficiently so that it may be handled without discomfort, and pour about 30 cc. of the warm, diluted acid through the reflux condenser into the flask. Heat the reaction mixture to boiling, and add about 10 cc. more of acid every minute or two until all is added. Keep the mixture actively boiling during the period of addition, lowering the flame only if the reaction of oxidation becomes vigorous enough to overtax the capacity of the condenser. In this way a moderated reaction is spread over several minutes; otherwise, without continuous boiling, the oxidation might be concentrated in one period of 30 to 60 seconds, with attendant flashes of fire inside the flask and boiling over of the contents of the flask. Now reflux the completed mixture for 30 minutes. If an appreciable amount of solid *p*-nitrotoluene collects in the condenser, shut off the water supply for a few moments, or until the temperature of the condenser rises above the melting point of *p*-nitrotoluene (51°).

After the reflux period, allow the reaction mixture to become cool. Dilute with 100 cc. of water and filter in the Buechner funnel. Wash the solid product, which is crude *p*-nitrobenzoic acid, upon the filter with 50 to 100 cc. of water, and transfer it to a beaker. Add about 50 cc. of approximately 1N sulfuric acid and 0.5 g. of sodium acid sulfite, and heat the mixture to boiling. This operation extracts possible residues of chromium compounds as soluble chromic sulfate. Now cool the mixture and filter in the Buechner funnel. Wash the solid residue with about 50 cc. of cold water.

Dissolve as much as possible of the solid product in 175 cc. of water to which is added a slight excess of ammonium hydroxide (about 20 to 30 cc. of 6N). Add 1 g. of decolorizing carbon and boil the mixture until the odor of ammonia becomes very faint. Filter, rejecting the solid residue of carbon and unchanged *p*-nitrotoluene. To the hot filtrate slowly add, with stirring, 50 cc. of 6N acetic acid, and allow the solution to stand until cold. Collect the resulting finely crystalline precipitate upon the Buechner filter, and wash it with 50 cc. of cold water. Dry the product for an hour at 100° to 120°. In the absence of a suitable oven, this drying operation may be conducted by spreading the *p*-nitrobenzoic acid crystals over the surface of an evaporating dish resting upon a beaker of boiling water, or even in a dish suspended in an oil bath at properly controlled temperature. Yield, 10 g. Melting point of pure *p*-nitrobenzoic acid, 240°.

This preparation may be recrystallized from glacial acetic acid; 80% alcohol has also been recommended.

Potassium permanganate may also be used for this oxidation (Ref. 26).

Optional Syntheses

290. 2,4-Dinitrobenzoic acid. Prepared by a similar method; see *Ind. Eng. Chem. Anal. Edition* **6,** 351 (1934).

p-**Bromobenzoic acid.** Prepared from *p*-bromotoluene, a product of the Sandmeyer reaction described in § 313. (See Ref. 40.) Similarly, *o*-**chlorobenzoic acid** (Refs. 10, 25, 27, 45) and **terephthalic acid** (Refs. 27, 30, 32, 34, 39).
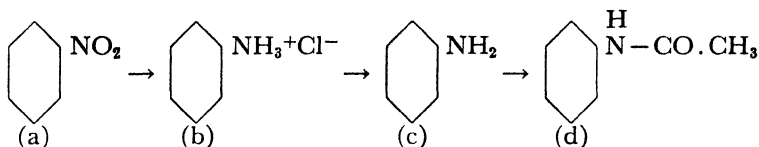
Adipic acid. Cyclohexanol is oxidized with nitric acid. The cyclo-paraffin ring is broken at the alcohol position, and an open-chain dibasic acid is produced (Refs. 5, 37).

Questions

1. What is the chemical reaction involved in the use of sodium bisulfite with the crude product?

2. If hydrochloric acid is substituted for acetic acid in precipitating the desired preparation, the product comes out as a fine powder instead of the more desirable coarser crystals. Why should this difference in state occur?

3. If the filtrate from the acetic acid reaction is treated with hydrochloric acid, a small additional yield of *p*-nitrobenzoic acid is obtained. Why might this be expected?

4. What conclusion might one draw as to any properties of *p*-nitrobenzoic acid from the fact that this additional yield is actually very small?

5. If the crude nitrobenzoic acid is dissolved in a considerable *excess* of ammonium hydroxide, and the mixture is acidified with acetic acid without prior expulsion of the excess ammonia, little or no precipitate is obtained. Why?

6. How is it possible for the relatively weak acetic acid to expel the stronger *p*-nitrobenzoic acid from its salt?

EXPERIMENT 33

Reduction to Amine and Acetylation
Aniline and Acetanilide

$$\underset{(a)}{\bigcirc NO_2} \rightarrow \underset{(b)}{\bigcirc NH_3^+Cl^-} \rightarrow \underset{(c)}{\bigcirc NH_2} \rightarrow \underset{(d)}{\bigcirc \overset{H}{N}-CO.CH_3}$$

291. When an aromatic nitro compound, such as nitrobenzene or one of the nitrotoluenes, is treated with an active metal such as tin in the presence of hydrochloric acid, the oxygen of the nitro group is replaced with hydrogen. The nitro radical is thus converted into the basic amine group, $-NH_2$. The newly produced amine immediately unites with excess hydrochloric acid to form the hydrochloride salt; but the addition of alkali, after the main reaction is complete, frees the desired amine, ready for separation and purification.

In aqueous solution, buffered with alkali, aniline reacts almost instantaneously with acetic anhydride to form the substituted amide, acetanilide. In order that this reaction may proceed neatly in one clear solution, aniline is reconverted into the salt form (compound (*b*) above), where it remains while the acetic anhydride is being dissolved and thoroughly intermixed. Addition of mild alkali then rapidly produces in turn (*c*) and (*d*). There should be no delay while acetic anhydride is in contact with water. (Method of Lumière and Barbier, 1905.) Note furthermore that vapors of aniline are toxic and should not be allowed to escape into the atmosphere of the laboratory. (See § 285.)

292. Aniline. To a mixture of 9 g. of granulated ("mossy") tin and 5 g. of nitrobenzene in a 200- or 300-cc. flask add slowly in 10-cc. portions 30 cc. of conc. hydrochloric acid. If the acid should boil actively, dip the body of the flask in a pan of cold water, moderating the temperature so that the reaction mixture is barely at the boiling point. Mix the reagents thoroughly from time to time by a swirling motion of the flask. As the reaction abates, place the flask in a boiling water bath for ten minutes or more. Care should be

taken that all of the nitro compound is reduced. Hold the flask up to the light, with eyes below the surface of the reacting solution. Look for possible oily drops of unchanged nitrobenzene at the surface. Any unreduced material will introduce a colored nitro-amine addition compound into the amine preparation, while incompletely reduced material (such as azobenzene or azoxybenzene) will cause a yellow or orange coloration. The solution, containing reactive stannous chloride, should be distributed from time to time all over the inside walls and neck of the flask, so as to reach all oxygen-containing material. The odor of nitrobenzene, noticeable during the first 30–45 minutes of the reaction period, finally disappears. If convenient, the mixture may be set aside until the next day, with still greater assurance of complete reduction. Additional delay of a week or two does no harm. In any case the newly-formed aniline salt is likely to crystallize with tin chloride as a double salt as soon as the reaction mixture cools, but no complication is introduced by such an occurrence.

The final reaction mixture is placed in the central flask of a steam-distillation outfit (§ 43). This flask may be of any size from 3/4-liter to 2-liter. Add 15 cc. of water and 20 g. of solid sodium hydroxide, and pass steam at moderate speed through the mixture. Note that at first the aniline comes over at so rapid a rate that the accompanying water is unable to dissolve all of it in the condenser. Accordingly oily globules of the free amine appear.

293. Acetanilide. Soon the production of oily globules ceases, and subsequent distillation yields the balance of the product as a clear aqueous solution. When a total of 100 cc. of distillate has been collected, it may be assumed that the organic product is completely distilled. To this distillate add a quantity of the dilute hydrochloric acid of the laboratory just sufficient to react with all of the amine, assuming 100% yield. The resulting solution should be clear and not above room temperature. Now dissolve 0.05 mole of acetic anhydride in the reaction mixture, and immediately add 0.05 mole of sodium acetate (either hydrate or anhydrous). Stir well, filter, wash the crystalline product with cold water, and dry. Yield, about 3 g. Melting point of pure acetanilide, 114°.

294. _p_-Toluidine. Substitution of _p_-nitrotoluene for nitrobenzene in § 292 gives _p_-toluidine, which in turn is converted into

aceto-*p*-toluidide, m. p. 152°. Since *p*-toluidine is a solid (m. p. 45°) it may crystallize in the condenser used in steam distillation, but is easily melted by stopping the current of cooling water in the condenser jacket for a few moments.

295. Aniline with Ether Extraction. If supplies of material permit, the procedure of § 292 may be run on a larger scale, using a 1-liter flask fitted with an air-cooled condenser. The following quantities of reagents are appropriate: 55 g. of mossy tin, 30 g. of nitrobenzene, 150 cc. of conc. hydrochloric acid, and 90 g. of solid sodium hydroxide. The resulting steam distillate is treated as follows.

Saturate the distillate—aniline and water together—with clean, fine granulated or powdered salt, and extract the aniline with a total of 100 cc. of ether, divided into such portions as you think advisable. (See also Chap. 8.) Dry the combined ethereal extracts with 6 to 8 g. of coarsely broken pieces of potassium or sodium hydroxide (not powder). After the solution is dry remove the drying agent, taking care to eliminate the few drops of highly concentrated caustic alkali solution which may have been produced.

It is now important to note the difference in technique when diethyl ether has been used, in contrast to that employing diisopropyl ether. Diethyl ether is dangerously inflammable. Read § 34 carefully before proceeding; then distil the ethereal aniline solution in the appropriate manner until the ether has been removed. See § 90 for discussion of technique where a small volume of product is to be separated from a large volume of extract.

The ether recovered from the experiment should be placed in a stock bottle or can marked "Recovered Ether," or given to the next student requiring a supply.

After the ether has been expelled, replace the water-cooled condenser with an air-cooled condenser and distil the final product of aniline. If the distillate is of decidedly yellowish-orange color, it may sometimes be improved by redistillation from the same distilling flask in the presence of a pinch of aluminum or zinc dust. Distillation under reduced pressure in the presence of the metallic dust is often effective. In any case, however, the product, even if colorless when freshly prepared, will become dark on standing. Yield, 20 g. Boiling point of aniline, 184.4° (cor.).

Optional Syntheses

296. m-Nitroaniline. Reduction of one of the two nitro groups of a dinitro compound with the aid of a mild reducing agent (sulfide ion). (Refs. 24, 26, 27, 28, 30, 34, 35, 37, 38, 39, 43, 45.)

p-Aminodimethylaniline. A more difficult synthesis, involving reduction of either p-nitrosodimethylaniline (§ 320) or methyl orange (§ 327). May be converted into methylene blue (Refs. 24, 27, 30, 34, 35, 36).

Ethylaniline. Illustrates the alkylation of aniline upon the nitrogen (Refs. 32, 40).

Questions

1. Why is it necessary to add sodium hydroxide before steam distillation is carried out?

2. What can you judge of the vapor pressure of aniline, based on your experience in the steam distillation of the substance?

3. Why must nitrous acid vapors be excluded from an amine preparation?

4. Suppose you had used tin and hydrochloric acid in the preparation of an amine which was not volatile in steam, although it was soluble in water. Devise a method of isolating the product.

5. Tin has two valence changes, $Sn \rightarrow Sn^{++} \rightarrow Sn^{++++}$, during the aniline reaction. Why might this be considered favorable in contrast with zinc, which has only one valence change, $Zn \rightarrow Zn^{++}$?

EXPERIMENT 34

β-Phenylhydroxylamine

(Reduction of Nitrobenzene in a Solution of Low Acidity)

$$C_6H_5NO_2 + Zn \xrightarrow{\text{(H}_2\text{O)}} C_6H_5NHOH + ZnO$$
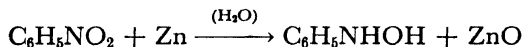
297. In neutral or nearly neutral aqueous solution, nitrobenzene is reduced by zinc to the aryl hydroxylamine, an unstable compound which should be converted into a derivative at once. In alkaline solution a hydrazobenzene is formed. These variant products are the result of the differing reduction potential of the zinc in solutions of widely different pH value.

In a 2-l. flask equipped with a mechanical stirrer and a thermometer, place 12.5 g. of ammonium chloride, 400 cc. of water, and 25 g. of nitrobenzene. Stir the mixture vigorously, and add during a 15-minute period 40 g. of high-grade zinc dust. The addition of zinc dust should be rapid enough so that the temperature rises rapidly to about 55° or 60° and remains in this range until the zinc has all been added. When the temperature starts to fall, filter the reaction mixture, and saturate the filtrate with clean common salt. Wash the zinc oxide precipitate with 50 cc. of warm water and treat the washings with salt also, thus getting a small additional yield. β-Phenylhydroxylamine crystallizes in feathery needles, and is collected on filters after the crystallizing mixtures have stood for an hour in the ice bath. Proceed at once to convert the product into whatever secondary preparation is desired.

298. Nitrosobenzene. Dissolve 12 g. of β-phenylhydroxylamine in 300 cc. of ice-cold 6N sulfuric acid contained in a 1.5- or 2-l. flask. Dilute the solution with 500 cc. of ice water, and run in rapidly a solution of 12 g. of sodium dichromate (dihydrate) in 200 cc. of water, with intermittent shaking, and cooling of the flask in an ice bath. Nitrosobenzene is precipitated, collected on the Buechner funnel, washed with water, and distilled in steam. The resulting purified nitrosobenzene, while white or colorless in

254

the solid state, is green when liquid.   It may be recrystallized from a very small volume of alcohol.   M. pt., 68°.

299. Cupferron.   The phenylhydroxylamine may be converted into the valuable analytical reagent ammonium nitrosophenylhydroxylamine ("Cupferron") with the aid of sodium nitrite and hydrochloric acid (Refs. 4, 30, 35).

Optional Syntheses

300. Hydrazobenzene.   Nitrobenzene is reduced in alkaline solution, using zinc dust.   The product may be used in the benzidine rearrangement (Refs. 23, 24, 27, 28, 30, 32, 34, 35, 37, 41, 43, 45.

EXPERIMENT 35

Sulfonation

301. In a reaction somewhat suggestive of nitration, one hydroxyl group is displaced from the molecule of sulfuric acid, and the residue SO_3H, known as the sulfonic group, replaces hydrogen in an aromatic compound. Ordinary concentrated acid is often employed, and in more troublesome cases the more active "fuming" acid (§ 447) is necessary.

When the aromatic compound which is to undergo this sulfonation reaction is an amine, there is first an immediate reaction to form the salt. Prolonged heating transforms such a salt into the amino sulfonic acid, a compound whose structural formula may be represented directly as the name implies, or as the inner salt:
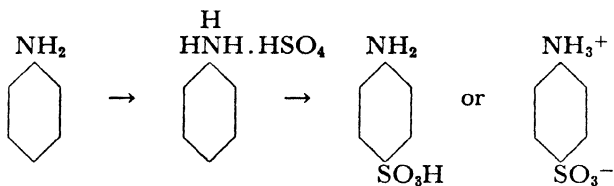
302. Sulfanilic Acid. When aniline is subjected to the sulfonation reaction the rules of orientation would predict the formation of ortho and para sulfonic acids. At about 180°, however, the ortho-derivative either does not form, or is rearranged and transformed into the para compound. As a result, the single para compound, known to the trade simply as "sulfanilic acid," is obtained.

Place 0.2 mole of freshly distilled aniline in a 200-cc. flask, using a funnel to avoid wetting of the neck of the flask with the aniline. Remove the funnel, and cautiously add 30 cc. of conc. sulfuric acid. Heat the mixture in the open flask for 4 to 5 hours in an oil bath, keeping the temperature of the oil between 180° and 190°. The reaction is complete when a sample of 1 or 2 drops of the liquid is completely dissolved by 3 to 4 cc. of 2N sodium hydroxide solution without leaving the solution cloudy.

Cool the mixture to 50° or below and pour it with stirring into 200 g. of cold water or of crushed ice. Collect the precipitated mass of crude sulfanilic acid upon the Buechner filter, wash with cold water, and dissolve in the least possible amount of boiling water. Add 2 to 3 g. of decolorizing carbon to the boiling solution and filter through a fine-grained filter paper upon the Buechner funnel. Upon cooling, the solution deposits crystals which contain one molecule of water of crystallization. Should the temperature of the solution be reduced much below room temperature, however, a dihydrate may also crystallize. The substance does not melt sharply, and no attempt should be made to estimate melting point. Yield, 15 g.

If the product is dark colored (owing to carelessness in regulation of the oil-bath temperature), it may often be purified to advantage in alkaline solution, as follows: Dissolve the impure solid in as small an amount as possible of warm 2N sodium hydroxide solution, add decolorizing carbon, boil 3 minutes, and filter. To the filtrate then add an amount of conc. hydrochloric acid slightly more than the quantity chemically equivalent to the sodium hydroxide used. Collect the resulting precipitate on a Buechner filter and recrystallize from the minimum volume of boiling water.

Care should be taken not to expose moist crystals of sulfanilic acid to air containing oxides of nitrogen during the drying process; otherwise the compound may be superficially diazotized and converted into colored material.

Questions

1. What is the general value of introducing the sulfonic acid radical into an aromatic compound?

2. What is the scientific basis for the test for completeness of reaction given in the sulfonation experiment which you conducted?

3. What effect does the entrance of the sulfonic acid group have upon the strength of aniline as a base?

EXPERIMENT 36

p-Nitrotoluene-*o*-Sulfonic Acid (Potassium Salt)

303. In a 500-cc. flask, suspended in a water bath at room temperature, place 20 g. of *p*-nitrotoluene and 30 cc. of (20%) fuming sulfuric acid, and mix well. After the mixture has stood for 10 minutes, slowly heat the bath to the boiling point. The reaction is complete when 5 drops of the mixture dissolve completely in about 5 cc. of water. The reaction mixture should not be heated above 100°.

Now pour the mixture into 550 cc. of water. Decolorize the resulting solution with carbon by the standard procedure (§ 109) and neutralize the filtrate by the cautious addition of the requisite quantity of solid potassium carbonate. A change in color from light yellow to brownish marks the neutral point. Heat the resulting mixture until any precipitate dissolves. Upon cooling, the desired potassium salt crystallizes in yellowish-brown needles along with a little potassium sulfate. Recrystallize from boiling water. The purified product is light yellow.

Derivatives. Interesting sequences of preparations may be arranged to follow this sulfonation experiment. The methyl group may be oxidized (see method of § 289) to the carboxyl group, and the nitro group then reduced—or the oxidation step may be omitted. An amine thus prepared is then diazotized and converted into various azo dyes (§ 321) which are acidimetric indicators.
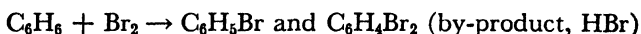
Optional Syntheses

304. Benzene sulfonic acid may be prepared by the sulfonation of the hydrocarbon (Refs. 23, 24, 27, 30, 34, 35, 37, 39, 40, 43).

p-**Toluene sulfonic acid** (Refs. 30, 31, 35, 39).

p-**Bromobenzene sulfonic acid** (sodium salt) (Ref. 23).

EXPERIMENT 37

Bromobenzene and *p*-Dibromobenzene

$$C_6H_6 + Br_2 \rightarrow C_6H_5Br \text{ and } C_6H_4Br_2 \text{ (by-product, HBr)}$$

305. The replacement of hydrogen in benzene by bromine is greatly accelerated by the presence of the catalyst ferric ion, introduced conveniently by the addition of metallic iron to the reaction mixture. In addition to the monobromo derivative, dibromobenzenes are produced; mostly the para isomer, a small amount of ortho, and a very small amount of meta.

To a 500-cc. round-bottomed flask attach a dropping funnel and a water-cooled reflux condenser. The arrangement illustrated in § 355 is suitable, or a standard three-necked flask may be employed. If neither of these outfits is available, provide a doubly bored cork in a simple flask. Connect the top of the reflux condenser to an inverted funnel suspended over water as shown in § 368. Now place in the flask 0.35 mole of benzene and two or three shingle nails, or 2 to 3 g. of tacks. After special care is taken that the stopcock of the dropping funnel is properly lubricated and securely fitted (danger to fingers!), pour 0.5 mole of chilled bromine, taken from the refrigerator, through a small funnel into the dropping funnel.

Gently heat the benzene nearly to the boiling point, and remove the burner. Start running in the bromine slowly, with constant caution not to allow bromine to leak out at the stopcock. The addition may now be as rapid as possible without excessive ebullition of the reaction mixture.

On account of the great stability of the bromine derivatives of benzene, there need be no fear of interrupting this experiment at any point in the subsequent procedure. If the mixture is allowed to stand for a day or more, the residual bromine will be used up, and thus the next procedures will involve less vapor nuisance. Finally, at the end of the period of bromination, boil the reaction mixture for 5 minutes.

Wash the crude mixture with several portions of water. Either of two plans of purification may now be followed according to time available. The first (§ 306), involving fractional steam distillation, gives a neater separation of the two desired compounds, but is time consuming. Otherwise follow § 307. In any case, note vapor-pressure data in § 445.

306. Fractional Steam Distillation. The crude wet product is steam-distilled from a flask of at least 1 1/2 l. capacity in the manner employed with aniline. As soon as crystals appear in the condenser, change to a second receiver and continue distillation.

The first distillate is mainly bromobenzene with accompanying water. The second is principally p-dibromobenzene. Separate the first product, dry over anhydrous calcium chloride or magnesium sulfate, and distil from a small distilling flask, collecting the product coming over between 150° and 160°. Yield, 30 g. Boiling point of pure bromobenzene, 156°. Recrystallize the solid dibromobenzene from ethyl alcohol of 80 to 90% grade. Melting point of p-dibromobenzene, 89°.

307. Ordinary Fractionation. After thorough washing with water to remove hydrobromic acid, separate the oil and dry over anhydrous calcium chloride, magnesium sulfate, or well-dried anhydrous sodium sulfate. Distil the product into four receivers in the manner described in § 73 with the aim of separating the mono- and dibromobenzene fractionally. After repeated distillations nearly all of the final distillate should be found in the first and fourth flasks. The first is of course bromobenzene, the last p-dibromobenzene. The fact that the latter is normally a solid may necessitate modification of the ordinary technique of fractional distillation.

Optional Syntheses

308. p-Bromoacetanilide. This is prepared by direct bromination (Refs. 23, 24, 27, 31, 38). Similarly, 4-bromo-aceto-p-toluidide (Ref. 23).

m-Bromobenzoic Acid. A good example of a case where bromination requires an elevated temperature, introducing the technique of conducting a reaction under pressure in a so-called "bomb" of heavy glass tubing (Refs. 27, 32, 37).

Iodobenzene. Direct iodination of benzene is practicable only with aid of nitric acid (Refs. 9, 26).
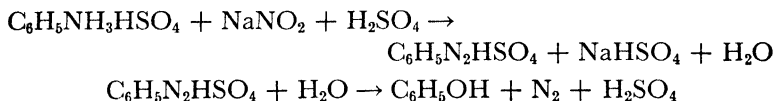
Questions

1. How may a "theoretical yield" be calculated from an experiment such as the preparation of bromo and dibromobenzene?

2. On the basis of the vapor-pressure tables in the Appendix, explain why fractional distillation in steam is more effective here than simple fractionation in the absence of water. Would a change to reduced-pressure technique affect this situation?

See also question 6, Chap. 8.

EXPERIMENT 38

Phenol

$$C_6H_5NH_3HSO_4 + NaNO_2 + H_2SO_4 \rightarrow$$
$$C_6H_5N_2HSO_4 + NaHSO_4 + H_2O$$
$$C_6H_5N_2HSO_4 + H_2O \rightarrow C_6H_5OH + N_2 + H_2SO_4$$

309. From a structural standpoint, the essential feature of the first equation given above is the replacement of the three hydrogen atoms of the substituted ammonium group ($-NH_3^+$) by one atom of nitrogen derived from nitrous acid. This is the reaction known as "diazotization." It is followed here by simple decomposition and replacement of the diazo group ($-N \equiv N^+$) by hydroxyl, yielding phenol. Low temperature is essential for diazotization, boiling temperature for the second process.

In a 400-cc. beaker place 150 g. of crushed ice (200 g. in warm weather) and 18 cc. of conc. sulfuric acid; then add with effective stirring 14 g. (0.15 mole) of purified (that is, light yellow or colorless) aniline. After the aniline has been added, introduce in small portions, with stirring, 12 g. of sodium nitrite. Now allow the reaction mixture to stand in an ice bath (0 to 3°) for 10 minutes; then add 2 g. of urea to remove the excess nitrous acid.

In a 1-l. distilling flask place 300 cc. of water, and add 20 cc. of conc. sulfuric acid. Including this flask, assemble apparatus like that pictured in Fig. 4, § 33. Now heat the sulfuric acid solution to boiling, and pass in the diazonium salt solution through the funnel as fast as possible without flooding the mixture so as to interrupt boiling or causing foam to rise up into the neck of the flask. Note carefully that the mere evolution of small bubbles of nitrogen is not boiling. In other words, keep the temperature up in the vicinity of 100° and see that steam is being expelled in quantity into the condenser.

As the distillation proceeds, keep the reserve supply of diazonium salt solution ice cold until a portion is needed in the dropping funnel.

Although phenol may also be produced without all of the precautions above cited by mere warming of the solution to room temperature, excessive production of tarry by-products occurs.

After all of the diazonium solution has been run in, continue distillation until 350 to 400 cc. of distillate has been collected. Saturate this distillate with common salt. Read discussion of extraction (§ 88) and use a 200-cc. supply of ether in an effective manner to extract the phenol. Ethyl ether gives the best product, but isopropyl ether is safer and is acceptable. Now dry the combined extracts over anhydrous magnesium sulfate.

Warning. Phenol ("carbolic acid") is injurious to the skin, and will cause painful burns. If the substance gets upon the skin, wash at once thoroughly. If irritation develops from exposure to phenol, consult the instructor or a physician.

In view of the fact that the extract contains far more solvent than phenol, read § 90 describing special technique in separating the components of such a mixture. Now remove the ether by an appropriate mode of distillation. Replace the condenser with one of air-cooled type and distil the residue. The fraction boiling between 176° and 182° is collected as phenol. Yield, 8 g. Boiling point of pure phenol, 182°; melting point, 41°.

310. Reactions of Phenol. Dissolve approximately 1 g. of phenol in 15 cc. of water, and use this solution in tests (*a*) to (*e*).

(*a*) Test the reaction of phenol with neutral litmus paper.

(*b*) Add one drop of dilute sodium hydroxide and one drop of phenolphthalein indicator to 10 cc. of water. Treat 3 cc. of this solution with 1 or 2 cc. of your phenol solution.

(*c*) Repeat (*b*), using methyl orange instead of phenolphthalein, and explain difference in behavior.

(*d*) Add bromine water slowly to a 5-cc. sample of the phenol solution. What is the white compound?

(*e*) Add a few drops of ferric chloride solution to 3 cc. of the phenol solution.

Optional Syntheses

311. β-Naphthol. This analogous derivative of the naphthalene series is usually prepared by the alkaline fusion of a sulfonate instead of diazotization of an amine (Refs. 27, 28, 30, 31, 32, 34, 35, 43).

Hydroquinone (*p*-Dihydroxybenzene). This valuable photographic developing agent may be prepared by reduction of the corresponding ketone (benzoquinone) (Refs. 27, 30, 32, 34, 35, 37, 40, 43). The reverse reaction is described in § 345.

Anisole (Methyl Phenyl Ether) may be prepared by methylation of phenol (Refs. 27, 30, 32, 33, 35, 37, 38, 39, 40).

Salicylic Acid (*o*-Hydroxybenzoic Acid). This important industrial product is made by introduction of carbon dioxide into an alkaline phenol mixture (Refs. 24, 27, 30, 34, 35, 37, 43).

Questions

1. Suppose hexylamine were substituted for aniline in this experiment. What difference in behavior of the materials would you expect?

2. What objection would there be to mixing the nitrite and sulfuric acid, and then adding this mixture to the aniline and ice?

3. How could you modify this experiment to prepare bromobenzene instead of phenol?

4. Why does the undissolved phenol in the original reaction distillate remain as a liquid, whereas the melting point of phenol is 10° or 20° higher than the temperature of the distillate and receiver?

5. Which do you think could be more easily extracted from aqueous solution, phenol or aniline?

6. Why does benzoic acid dissolve freely in sodium bicarbonate solution, whereas phenol does not?

7. In the distillation of the original reaction mixture, why does not the volatile component, water (b. pt. 100°), nearly all pass over first, and finally the less volatile component, phenol (b. pt. 182°)? (See § 71.)

8. Why is it desirable that the ethereal extract be slowly distilled, instead of rapidly, as the temperature approaches 170°?

9. What happens when phenol is distilled with zinc dust?

DIAZO REACTIONS

312. In each of the following experiments **diazotization** is the introductory operation. Normally a primary aromatic amine is first dissolved in at least three times its equivalent of hydrochloric or sulfuric acid. One equivalent of acid forms the amine salt; a second reacts shortly with one mole of sodium nitrite, to produce as needed the desired nitrous acid; and the third (or greater excess) maintains the high acidity required to prevent the newly formed diazonium salt from going astray into by-products.

From aniline as an example, benzene diazonium chloride is the product of diazotization:

$$C_6H_5NH_2 \rightarrow C_6H_5NH_3{}^+Cl^- \rightarrow C_6H_5N_2{}^+Cl^-$$
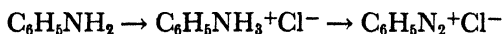
Equimolal quantities of amine and sodium nitrite are usually required, since an excess of either may cause secondary reactions. Usually temperatures above 5° are avoided lest there be deomposition of the reactive diazo product; while temperatures below 0° are likely to involve too slow a reaction rate. If a beaker is used for diazotization, ice should be placed both inside and outside, since the reaction produces considerable heat, and it is difficult to agitate a solution in a beaker sufficiently to effect thorough mixing and cooling. The process is more easily carried out in a flask if ice be not admissible in the reaction mixture.

Occasionally the amine is amphoteric, as in the case of § 326, thus introducing the complication of an inner salt and causing considerable change in the technique of diazotization.

One of the simpler products of the diazo method has already been described as an elementary experiment (phenol, § 309). Other illustrations follow.

Do not interrupt any experiment involving diazotization from the time that the formation of the diazonium salt starts until that compound is completely transformed into the desired derivative, such as phenol, aryl bromide, dye, etc. Never attempt to keep a diazonium salt overnight, even in a refrigerator.

EXPERIMENT 39

p-Bromotoluene

313. *p*-Bromotoluene; Sandmeyer Reaction. When the solution of an aryl diazonium salt, such as benzene diazonium sulfate, is heated with a mixture of a cuprous halide and the corresponding halogen acid, the diazonium group is replaced by halogen, with release of nitrogen gas.

$$CH_3C_6H_4.N_2.HSO_4 + Cu_2Br_2 + HBr \rightarrow$$
$$CH_3C_6H_4Br + N_2 + Cu_2Br_2 + H_2SO_4$$
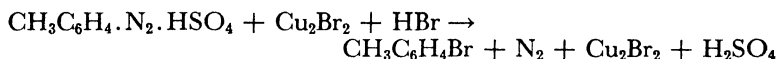
In a 1-l. flask mix 0.4 mole (42.8 g.) of *p*-toluidine and 350 cc. of water, and then add 45 cc. of conc. sulfuric acid. Warm the mixture if necessary to get all reagents dissolved, and provide an ice bath large enough to permit the flask to be effectively cooled by shaking in the ice slush. A handful of salt should be added to the ice.

Cool the toluidine sulfate solution to about 0°, and very slowly add a solution of 30 g. (a slight excess) of sodium nitrite in 50 cc. of water. Keep the temperature of the diazotization reaction between 0° and 5° with the aid of effective shaking in the ice bath, and allow the completed mixture to stand 30 minutes. During all of this time it must remain in the ice bath. In the meantime, prepare cuprous bromide as follows.

Divide into two equal parts a solution of 0.5 mole (125 g.) of cupric sulfate (hydrate) in about 600 cc. of water. Into one part stir 0.25 gram-atom (16.3 g.) of zinc dust. If the blue color persists— indicating impure zinc and thus an inadequate quantity—add just enough zinc to complete the reaction. Decant the liquid; wash the precipitate of copper with dilute sulfuric acid to remove possible excess zinc, and decant the liquid again. Now add to the copper the second portion of cupric sulfate, 1.0 mole of potassium or sodium bromide, and 15 cc. of conc. sulfuric acid. Stir well. The white precipitate is cuprous bromide, Cu_2Br_2.

Mount a 2-l. flask in the customary position for steam distillation

and introduce a third tube (7 to 9 mm. in diameter) leading almost to the bottom of the flask. Attach a small funnel to the outer end of this tube. Now place the cuprous bromide-acid mixture in the flask and heat to boiling.

Through the funnel tube slowly introduce from a dropping funnel the *p*-toluene diazonium sulfate solution while steam is passed rapidly through the mixture. Continue the distillation for an hour or more, or until frothing ceases and no further yield of oily product comes over.

Add 20 cc. of 6N sodium hydroxide to the aqueous distillate to extract *p*-cresol from the product, shake well, and isolate the crude bromotoluene. Wash the product once with concentrated sulfuric acid, then with sodium hydroxide and finally with water. Should the product solidify, warm the wash liquids slightly before use. A yellow or brown color may often be removed by washing with stannous chloride solution.

Dry the product over magnesium sulfate or calcium chloride, filter, and distil through an air-cooled condenser, preserving the fraction boiling between 178° and 186°. Yield, 35 g. Boiling point of pure *p*-bromotoluene, 184°; melting point, 26°.

Optional Syntheses

314. Chlorotoluenes. Cuprous chloride is substituted for the bromide of the foregoing experiment (Refs. 3, 23, 24, 27, 28, 30, 31, 37, 43).

p-**Tolyl Cyanide and *p*-Toluic Acid.** Cuprous cyanide is substituted for the bromide, yielding a nitrile which is hydrolyzed to give an aromatic acid (Refs. 24, 27, 33).

p-**Iodotoluene.** Iodine is introduced without the necessity of a cuprous salt (Ref. 27).

Questions

1. Suppose heptyl amine, $C_7H_{15}NH_2$, were substituted for the toluidine ($C_7H_7NH_2$) in the above experiment. What trouble might be expected?

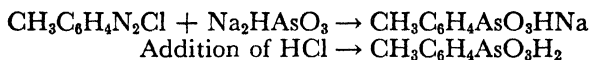**2.** Explain the value of sodium hydroxide in purifying the steam-distilled bromotoluene.

3. Do you think that this preparation requires a specially good drying agent? Why?

4. How could you distinguish the product, by chemical reaction tests, from *α*-bromotoluene, its isomer?

5. Why is sulfuric acid used here instead of hydrochloric acid?

OPTIONAL EXPERIMENTS

315. Aromatic Arsenical Compound. The Bart Reaction. In a reaction resembling the Sandmeyer synthesis (§ 313), an aryl diazonium salt, mixed with arsenite ion in the presence of a trace of a copper compound as catalyst, loses nitrogen and couples with the arsenite group to yield an aryl arsonic acid, of type formula $Ar-AsO_3H_2$.

$$CH_3C_6H_4N_2Cl + Na_2HAsO_3 \rightarrow CH_3C_6H_4AsO_3HNa$$
$$\text{Addition of HCl} \rightarrow CH_3C_6H_4AsO_3H_2$$

p-**Tolylarsonic Acid.** To 100 cc. of water add 32 g. of anhydrous sodium carbonate, 18 g. of arsenious oxide, 1 g. of crystalline cupric sulfate, and 3 g. of sodium formaldehyde sulfoxylate (also a catalyst). Heat to boiling to dissolve the solids, and cool the solution to 0°.

Following somewhat the technique of § 313, diazotize 0.125 mole of *p*-toluidine, using the minimum permissible quantity of hydrochloric acid (2 1/2 times 0.125 mole). Enough ice is included in the mixture undergoing diazotization to bring the final volume of the *p*-tolyl diazonium chloride solution to 200 or 225 cc.

To the arsenical mixture previously prepared add 10 cc. of benzene (to reduce frothing) and slowly stir in the diazonium salt solution, keeping the temperature below 5°. Allow the mixture to stand 20 minutes in the ice bath, and then 1 hour in the open, with frequent and thorough stirring. Now heat to 50° or 60°. Gas is evolved, and tar coagulates. Cool the mixture, filter, and evaporate the filtrate to one-third of its former volume. Add 1 to 3 cc. of conc. hydrochloric acid a few drops at a time, or as long as tar separates. Filter again and add 30 cc. of conc. hydrochloric acid, thus precipitating *p*-tolylarsonic acid. With the aid of decolorizing carbon, recrystallize from boiling water. About 100 cc. will be required. Yield, 4 g.

316. Arseno Derivatives. The presence of a soluble aromatic arsenical derivative of this type may be detected by submitting a test-tube sample of a solution of the supposed arsenical to the following test. Heat with 1 g. of hypophosphorous acid; or saturate with sulfur dioxide and heat with 1 g. of phosphorous acid. An insoluble "arseno" derivative is promptly formed. Usually this is a characteristic amorphous yellow solid, in the present case arseno-*p*-toluene, $CH_3 . C_6H_4 . As = As . C_6H_4 . CH_3$.

Optional Syntheses

317. *o*-Nitrophenylarsonic Acid. Another illustration of the Bart reaction (Ref. 36).
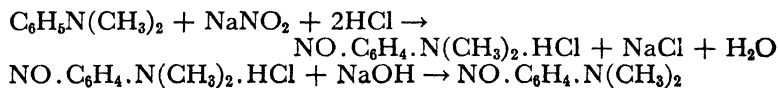
Arsanilic Acid. Direct arsenation of aniline (Refs. 3, 16, 30, 35).

Phenol-*p*-arsonic Acid (Sodium Salt). Direct arsenation of phenol (Refs. 4, 36).

Arsphenamine (Salvarsan). This famous arsenical drug, which is an arseno derivative, calls for considerable skill in preparation (Ref. 36).

318. Use of Borofluorides. Improved yields from Bart reactions are obtained through the use of diazonium borofluorides instead of the ordinary hydrochlorides (Ruddy, etc., 1942).

319. Nitroso Derivatives. The substitution of a dialkylaniline for aniline in a procedure arranged as though for diazotization yields instead of a diazonium salt a para-nitroso derivative, in which the nitrous acid is found to have reacted with the para hydrogen instead of the amine group. Being in acidic solution, the product appears in the form of a yellow hydrochloride. Upon addition of alkali the free base, a brilliant green compound, is obtained.

$C_6H_5N(CH_3)_2 + NaNO_2 + 2HCl \rightarrow$
$$NO.C_6H_4.N(CH_3)_2.HCl + NaCl + H_2O$$
$NO.C_6H_4.N(CH_3)_2.HCl + NaOH \rightarrow NO.C_6H_4.N(CH_3)_2$

320. *p*-Nitrosodimethylaniline. In a 500-cc. flask, cooled in an ice bath, mix 80 cc. of water, 45 cc. of conc. hydrochloric acid, about 20 g. of ice, and 20 g. of freshly distilled dimethylaniline. Now add very slowly from a dropping funnel a solution of 12 g. of sodium nitrite in 20 cc. of water, while shaking the flask and keeping the mixture thoroughly cooled in the ice bath. Allow the flask to stand for 1 hour in the cooling bath, and then collect the precipitate of *p*-nitrosodimethylaniline hydrochloride upon the Buechner filter. Place the product in a large evaporating dish, add 50 cc. of conc. hydrochloric acid, crush all lumps finely, and transfer the semisolid mass to the Buechner filter. Suck down and reject the discolored hydrochloric acid, and divide the resulting yellow crystalline mass into two equal parts.

Recrystallize one of the two portions from the minimum quantity (perhaps 150 cc.) of 2N hydrochloric acid, which is not heated over 80° during the process. Cool the solution, wash the crystalline product with 3N hydrochloric acid, and dry in the open air.

After crushing the second portion to a granular powder, free from lumps, place the material in a large separatory funnel with about 125 cc. of benzene. Now add, in 10-cc. portions, 1N sodium carbonate solution, shaking well after each addition. If this reaction is allowed to proceed too vigorously, as in the presence of too much alkali, the dimethylamino group will be removed by hydrolysis, causing an undue amount of the dark-red by-product *p*-nitrosophenol to appear.

When the yellow salt is completely converted into the benzene-soluble base, separate the benzene layer, dry it with anhydrous magnesium sulfate, filter, and evaporate to a volume of about 25 cc. Transfer the residual solution to a 250-cc. beaker and add 100 cc. of light petroleum solvent (boiling range below 120°). Heat to the boiling point on the steam bath, if necessary adding more solvent to effect complete solution. Cool, collect the crystalline product, and dry. Yield, 15 g. Melting point of *p*-nitrosodimethylaniline, 85°.

EXPERIMENT 40

Azo Dyes

321. Azo Dye. When an aromatic diazonium salt is treated with a suitable aromatic amine or phenol, usually with the aid of alkali of some kind, the two aromatic nuclei are united through the $- N_2-$ bridge, yielding an azo dye of type formula $Ar_1.N = N.Ar_2$ where Ar_1 and Ar_2 are any two of a great variety of benzene and naphthalene derivatives. The first example is simplest in theory, but somewhat more difficult practically than the second (methyl orange, § 327).

For example,

$$C_6H_5N_2Cl + C_{10}H_7NH_2(+ CH_3COONa) \rightarrow$$
$$C_6H_5N = NC_{10}H_6NH_2 + NaCl + CH_3COOH$$

322. Phenyl-azo-β-naphthylamine. As in many azo dye syntheses, this procedure calls for quantities closely agreeing with the equation. The aniline, sodium nitrite, and β-naphthylamine should be weighed to the accuracy of 20 mg. or better; otherwise a tarry preparation may be expected. This experiment definitely calls for careful technique and normally fails in the hands of nearly half of the students who try it!

Dissolve just 0.03 mole of light-colored or freshly distilled aniline in a mixture of 15 cc. of 6N hydrochloric acid and 10 cc. of water (equivalent to 0.09 moles of HCl), and place the resulting aniline hydrochloride solution in a 200- or 300-cc. (preferably long-necked) flask. Provide a slushy ice-and-water mixture containing enough salt to depress its temperature to about $-3°$.

With scissors or a sharp knife cut from the smallest available rubber tubing a slender rubber band, and place this band as a marker upon a thermometer at the 0° point. Insert the thermometer, so equipped, into the flask, and cool the aniline hydrochloride solution by means of the ice bath to about 0°. Now add slowly, a few drops at a time, but with thorough shaking of the flask, a solution of just 0.03 mole of pure sodium nitrite in 10 cc. of water. Keep the temperature of the reaction mixture between 0° and 5°.

While the resulting benzene diazonium chloride solution stands in the ice bath, dissolve just 0.03 mole of pure β-naphthylamine (Eastman's "white label" or equivalent) and 0.07 mole of sodium acetate (anhydrous or hydrate) in 100 cc. of alcohol which is heated under a water-cooled reflux condenser in a 500-cc. conical flask mounted in a water bath. Now cool the naphthylamine solution to about 30° to 35°.

To the naphthylamine solution add all at once, with vigorous shaking of the mixture, the diazonium chloride solution described above. Within a few seconds the azo dye forms and crystallizes suddenly. Now pour about 5 cc. of ice water into the flask from which the diazo solution has just been taken, for use in a later test, and return the flask to the ice bath. Reconnect the flask containing the dye to the reflux condenser, and heat to boiling, thus completely dissolving the dye. Remove the flask again, stopper it lightly, and set aside for slow cooling and crystallization. Collect the product on a Buechner filter, suck down the mother liquor thoroughly, and dry the crystals. Yield, 3 g.

Add the 5 cc. of washings left in the diazotization flask to a solution of a few crystals (0.1 g.) of β-naphthol in 15 cc. of dilute sodium hydroxide. An orange-red azo pigment is produced.

Mix 5 cc. of the alcoholic filtrate with 2 cc. of dilute hydrochloric acid, thus producing the red or acidic modification of the dye. To the remaining filtrate add 200 cc. of water, thus obtaining an additional yield of the yellow modification but of low purity.

Optional Experiments

323. *p*-Dimethylaminoazobenzene, Butter Yellow. This azo dye, prepared from benzene diazonium chloride and dimethylaniline, is used as an indicator to distinguish strong acids in the presence of weak acids. The above directions (§ 322) with but slight modification in volume of solvent will serve for this preparation.

324. Congo Red. An aromatic diamine (benzidine) is "tetrazotized" and coupled with a naphthalene derivative, yielding an azo dye used industrially, and of value as an indicator.
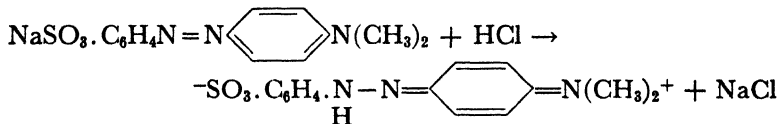
325. Paranitroaniline Red (Para Red). An azo pigment, sometimes called American Flag Red. Prepared by rapidly diazotizing *p*-nitroaniline at room temperature, and coupling the diazonium salt with β-naphthol.

Used in inexpensive red paints. Cloth may be treated with the diazonium salt solution, wrung out, and dipped into the naphthol solution, producing the color in the fabric. (Ref. 25.)

326. Amphoteric Compounds. The diazotization of an aromatic amino sulfonic acid leads to a diazonium inner salt instead of the usual chloride or sulfate as described in § 321. Occasionally such inner salt may even be isolated in crystalline form, as illustrated in § 328 below. In this example sulfanilic acid, which is conventionally represented as $HSO_3.C_6H_4.NH_2$, is designated by the inner-salt formula $^-SO_3.C_6H_4.NH_3{}^+$. Nitrous acid, in the presence of sulfuric acid, causes the three terminal hydrogen atoms to be replaced by an atom of nitrogen. Accordingly the substance is converted, without change of ionic charge, into the diazonium inner salt $^-SO_3.C_6H_4.N_2{}^+$. Addition of the coupling agent dimethylaniline, followed by sodium hydroxide, yields methyl orange:

$$^-SO_3.C_6H_4.N_2{}^+ + C_6H_5N(CH_3)_2 + NaOH \rightarrow$$
$$NaSO_3.C_6H_4.N = NC_6H_4N(CH_3)_2 + H_2O$$
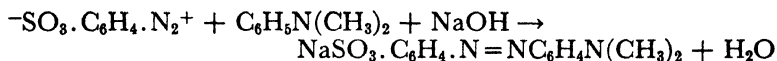
Treatment of methyl orange with a strong acid instantly transforms it into a red compound often called "helianthin." It is supposed that the proton from the strong acid unites with one of the azo nitrogen atoms, and that the necessary rearrangement of electrons—or bonds—in the molecule is responsible for the color change.

$$NaSO_3.C_6H_4N = N\langle\overline{}\rangle N(CH_3)_2 + HCl \rightarrow$$
$$\underset{H}{^-SO_3.C_6H_4.N - N} = \langle\overline{}\rangle = N(CH_3)_2{}^+ + NaCl$$

Helianthin is thus seen to be another inner salt itself. Actually it may be made by direct coupling in acid solution, and this method, while difficult to explain at the outset, is practically advantageous and is used below. Later the helianthin is neutralized, yielding methyl orange.

327. Methyl Orange; Preparation. Dissolve 0.05 mole of sulfanilic acid (monohydrate or anhydrous) in a solution of 9 cc. of 6N sodium hydroxide in 50 cc. of warm water. When all of the sulfanilic acid is dissolved, test the solution to be sure it is alkaline. In this solution dissolve 0.055 mole of sodium nitrite and cool the resulting mixture to about 30° C.

To about 150 g. of crushed ice in a 400-cc. beaker add 6 g. of concentrated sulfuric acid, and stir well. Now add the sodium sul-

fanilate solution in a fine stream with constant effective stirring. Mark the beaker for identification and set it away in the refrigerator or in an ice bath for an hour. If it is allowed to stand much more than 2 hours there is danger of decomposition of the diazonium salt.

In the meantime prepare a quantity of dimethylaniline acetate just equivalent to the maximum possible yield of diazonium salt which you calculate by theory. This acetate is prepared simply by mixing dimethylaniline with an equimolal quantity of glacial acetic acid.

328. Preliminary Test. At the end of an hour the maximum available yield of the diazonium inner salt should have precipitated in the beaker. A small amount remains in solution. As a preliminary experiment to illustrate the equations already given, decant about 5 cc. of the solution into a test tube. Make this alkaline with sodium hydroxide and immediately add 3 or 4 drops of the dimethylaniline acetate solution just prepared. Methyl orange at once is formed. Shake the test tube, and acidify the contents with hydrochloric acid. Helianthin is at once observed.

Now collect the precipitate of diazonium salt on a Buechner filter and wash it with a little ice water. Place the compound in a 400-cc. beaker, using about 25 cc. of ice water to aid in a complete transfer.

With vigorous, effective stirring, add the dimethylaniline acetate solution and stir until the resulting pasty mass is uniform in texture and color. The color should be a rich, deep reddish-purple. This operation requires about 10 minutes. Now add 18 cc. of 6N sodium hydroxide, stir well, and add 300 cc. of water. Heat this mixture to boiling, being careful to stir the mixture while heating to prevent bumping. If a clear deep orange-brown solution has not resulted, a little more water should be added.

The hot solution is now divided into two approximately equal portions, each of which is placed in a beaker. One portion is covered with a watch glass and set aside to cool slowly. Out of this separates the methyl orange, which is collected on a filter, washed with a little cold water, and dried in the open air. The other portion is treated as follows: 12 cc. of 6N hydrochloric acid is added very slowly with constant stirring. The beaker is then set aside to cool. When cold, the helianthin is collected, washed, and dried just as the methyl orange above. Total yield of two products, 10 g.

Optional Syntheses

329. Orange II. The diazonium salt of sulfanilic acid may be coupled with β-naphthol, yielding a water-soluble dye without the yellow-to-red indicator color transition (Refs. 28, 30, 43, 45).

Methyl Red. Diazotized anthranilic acid (*o*-aminobenzoic acid) is coupled with dimethylaniline, yielding the valuable indicator methyl red, which has a beautiful lemon yellow-to-red color change (Ref. 2).

Other azo dyes are cited in §§ 323–325.

Questions

1. What is the chromophore group in (*a*) methyl orange, (*b*) helianthin?

2. Explain how methyl orange acts as an indicator.

3. Show how you would prepare *p*-aminodimethylaniline from methyl orange.

4. What might happen to the diazonium inner salt if it were heated?

EXPERIMENT 41

Aryl Hydrazine

330. An aryl diazonium salt may be reduced to the corresponding aryl hydrazine. In this reaction the positively charged diazonium group $-N_2^+$ combines with four hydrogen atoms, the reducing agent furnishing the four necessary electrons, yielding the hydrazine ionic group $-NH-NH_3^+$. The resulting organic compound, in the presence of hydrochloric acid, is phenylhydrazine hydrochloride, $C_6H_5.NH.NH_3^+Cl^-$, a salt. Addition of alkali frees the base phenylhydrazine, $C_6H_5.NH.NH_2$. Either stannous chloride, or sodium sulfite, a less expensive reagent, is a satisfactory reducing agent for the purpose. Phenylhydrazine is toxic. If the substance comes into contact with the skin, wash thoroughly.

331. Phenylhydrazine Hydrochloride. In a 400-cc. beaker place 200 g. of crushed ice and 50 cc. of conc. hydrochloric acid. To this add slowly, with effective stirring, 18.6 g. (0.2 mole) of freshly distilled aniline. Now add in small portions with vigorous stirring 14.5 g. (an excess) of sodium nitrite. After the last portion of sodium nitrite has been added, place the beaker in an ice bath and allow to stand for 10 minutes.

While the above solution is standing, prepare a sodium sulfite solution as follows.

In a 1-l. beaker place 20 g. (0.5 mole) of technical flake sodium hydroxide and add 200 cc. of water. When the sodium hydroxide has dissolved, add 45 g. of sodium acid sulfite. (NOTE. The commercial acid sulfite is known as sodium metabisulfite, and has the formula $Na_2S_2O_5$.) Stir until the solid has dissolved, cool the resulting solution to 30° or below, and add 4 or 5 drops of phenolphthalein indicator solution. Now add, with stirring, still more sodium acid sulfite, a little at a time, until the pink color of the solution just disappears; then stir in an additional 5 g. (A total of 55 g. should be sufficient in all cases.)

Now cool this solution to about 15° in an ice bath, after which add 100 g. of crushed ice. When the temperature of this solution has fallen to 5°, add the benzene diazonium chloride solution very rapidly,

with stirring. The reaction mixture immediately turns to an orange-yellow color. Now slowly heat this solution on a water bath to 60° or 70°. Maintain this temperature for 30 to 60 minutes, during which time the color changes to a deeper shade of orange-red.

Now make the solution just acid to litmus, using concentrated hydrochloric acid; then heat on the water bath at 80° to 85° for 2 hours. (This heating does not have to be done all at one time.) During this time the color of the solution usually becomes much lighter, though not necessarily. While the mixture is still hot, take it outdoors, or to a hood, and add 200 cc. of conc. hydrochloric acid, with stirring. Now allow the solution to stand upon the laboratory desk for 10 to 20 minutes, during which time a quantity of coarsely crystalline phenylhydrazine hydrochloride will be precipitated. After the crystallization has been well advanced, place the mixture in an ice bath and cool it to 5° or below. This completes the crystallization; but if the cooling had been conducted rapidly, with ice, at first, an extremely finely divided precipitate might have been obtained. Filtration would be difficult.

Collect the phenylhydrazine hydrochloride upon the Buechner filter, press down well, and suck the residue as dry as possible; then wash with 10 cc. of 3N hydrochloric acid and again suck dry. Spread the crystals upon a piece of 6-inch filter paper and dry them. This preparation does not keep well if not well dried. The product from this method is usually pale yellow or faintly pink; pure phenylhydrazine is white. It may be purified by special recrystallization (Ref. 24), but this is not necessary for practical use of the compound.

332. Isolation of Phenylhydrazine. Although it is probably better to preserve this reagent in the form of its salt, the free base may nevertheless be readily prepared. To the hydrochloride add an excess of 4 to 6N sodium hydroxide. Extract the resulting phenylhydrazine with ether or benzene, dry over sodium or potassium hydroxide, expel the extracting solvent, and distil under reduced pressure. Boiling points—at 12 mm., 120°; at 18 mm., 137°.

Optional Syntheses

333. Nitro-derivatives. These are valuable as reagents in qualitative organic analysis. For example—*p*-nitrophenylhydrazine (Refs. 27, 30) and 2,4-dinitrophenylhydrazine (Refs. 13, 37).

Questions

1. What chemical reaction takes place when sodium acid sulfite and sodium hydroxide are mixed?

2. Explain how the sulfite can serve as a reducing agent.

3. Would an excess of nitrous acid be injurious in this reaction?

4. What is the reaction of phenylhydrazine with acetone?

5. Knowing that the free base phenylhydrazine, not the hydrochloride, reacts with the acetone, devise a method of use of our preparation to make the desired derivative of acetone.

EXPERIMENT 42

Reactions of Benzaldehyde

334. Cannizzaro Reaction. Benzaldehyde, in the presence of concentrated caustic alkali, is transformed by intermolecular oxidation and reduction into equimolal quantities of the corresponding alcohol and acid. The acid thus produced is of course converted into the alkali salt, from which it is readily recovered. The reaction is general for aromatic aldehydes, excepting ortho and para hydroxy derivatives.

$$2C_6H_5CHO + NaOH \rightarrow C_6H_5CH_2OH + C_6H_5COONa$$
$$C_6H_5COONa + HCl \rightarrow C_6H_5COOH + NaCl$$

In a 500-cc. flask mix together 40 g. of benzaldehyde, 50 cc. of di-isopropyl ether, and 40 cc. of saturated sodium hydroxide solution. Stopper the flask, shake the mixture at intervals during a half hour, and allow to stand for 24 hours or more. Now add just sufficient water to dissolve the sodium benzoate. Separate and preserve the ethereal layer, and extract the aqueous layer with 100 cc. more of the ether, used in three or four portions.

335. Benzoic Acid. Pour the aqueous residue into a beaker containing a mixture of 125 cc. of conc. hydrochloric acid and about 200 g. of ice. Recrystallize the resulting precipitate from water. Melting point of benzoic acid, 122.4°. Yield, about 22 g.

336. Benzyl Alcohol. Wash the combined ethereal extract with about 5 cc. of saturated sodium bisulfite solution, shaking thoroughly. Discard the bisulfite and any crystalline aldehyde-bisulfite compound which may have formed. Now wash the ethereal solution with two 10-cc. portions of N sodium hydroxide and dry it over anhydrous magnesium sulfate. Evaporate the ether, noting particularly § 34. Now distil the residue of crude benzyl alcohol, preserving the fraction boiling between 200° and 206°. Boiling point of pure benzyl alcohol, 205.8°. Yield, about 17 g.

337. Benzalacetone; Aldol Condensation. When an aldehyde is mixed with a ketone or aldehyde which has hydrogen attached to its alpha carbon atom, with mild alkali as a catalyst, the two molecules may then combine, carbon to carbon, yielding a substance of the "aldol" type. In the present case the aldol, if existent, is transitory. Presumably it loses water in the following manner, yielding benzalacetone:

$$C_6H_5.CHOH.CH_2.CO.CH_3 \rightarrow C_6H_5.CH=CH.CO.CH_3 + H_2O$$
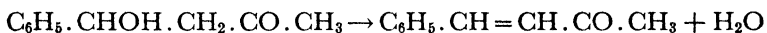
In a small flask place 25 g. of benzaldehyde, 50 cc. of acetone, and 25 cc. of water. With frequent shaking of the mixture, slowly add (over 15 to 20 minutes) from a dropping funnel 10 cc. of 3N sodium hydroxide solution, keeping the temperature below 35°. Allow to stand for a day or more. Next day add hydrochloric acid until the mixture is just acid to litmus. Isolate the oily layer, extract the aqueous layer with one 20-cc. portion of chloroform or benzene, and combine the oil and extract. Dry the oil-extract mixture over calcium chloride, transfer to a Claisen flask, evaporate the solvent, and distil under reduced pressure. The fraction distilling at 150° to 160° (30 mm.) is preserved. It should soon crystallize, yielding a slightly yellow product good enough for use in other work. The substance may be redistilled, or recrystallized from a very small volume of light petroleum solvent.

338. Benzoin Condensation. In the presence of cyanide ion, which seems to act as a catalyst, benzaldehyde undergoes an intermolecular reaction. The carbonyl group of one molecule of the aldehyde condenses with the carbonyl group of a second, yielding the keto-alcohol $C_6H_5.CHOH.CO.C_6H_5$, known as **benzoin.** The benzoin, like any typical secondary alcohol, may be oxidized to the ketone $C_6H_5CO.CO.C_6H_5$, known as **benzil.**

339. Benzoin. In a 500-cc. round-bottomed flask, equipped with a water-cooled reflux condenser, place a solution of 3 g. of sodium cyanide in 30 cc. of water. Add 30 cc. of acid-free or freshly distilled benzaldehyde and 50 cc. of 95% alcohol. Reflux the mixture from 30 to 45 minutes on the water bath. Upon cooling, crude benzoin crystallizes and is isolated on the Buechner filter. Wash the product first with a few cubic centimeters of alcohol and then with several portions of water. Benzoin may be recrystallized

from alcohol, but such purification is not necessary in the preparation of benzil.

340. Benzil. In the same apparatus used for the preparation of benzoin place the crude benzoin with three times its weight of conc. nitric acid (s.g. 1.42). With occasional shaking of the flask, heat the reaction mixture for 1 to 2 hours, or until evolution of oxides of nitrogen ceases. This operation should be conducted in a hood, or outdoors, or with protection of a funnel and beaker of alkali as pictured in § 368. (Note carefully the exact position of the funnel; not too deeply immersed.) Now pour the mixture into four or five times its volume of ice water and filter. Wash the yellow precipitate of crude benzil on the Buechner filter. Set aside about 1 *milligram* (estimated) of this preparation for use as seed crystals, and use the remainder for the subsequent experiment combining recrystallization with test of supersaturation.

341. Supersaturation Phenomena. In a large conical flask (500 to 700 cc.) place the crude benzil and an amount of 95% alcohol at the rate of 6.5 cc. for each gram of benzil used. Dissolve the benzil in the alcohol with the aid of the water bath, being very careful to leave no residual solid in any part of the vessel. Stopper the flask loosely, and set it aside to cool in a place where it will not be disturbed. When the solution has cooled to room temperature, drop in an exceedingly minute particle of solid benzil, taking care not to move or to disturb the flask. Beautiful yellow needles of purified benzil appear, and are eventually isolated and dried. Melting point of benzil, 95°. The velocity of crystallization, form of crystals, etc., may be varied neatly by slight changes in the 6.5-cc. value specified above.

342. Benzilic Acid; a Molecular Rearrangement. When benzil is heated in a solution of potassium hydroxide in dilute alcohol, a phenyl group shifts from one ketone group to the other. A molecule of water is added, and the substance benzilic acid (diphenyl hydroxy acetic acid) is produced in the form of its potassium salt.

$$C_6H_5CO.CO.C_6H_5 \rightarrow (C_6H_5)_2COH.COOK \rightarrow$$
$$(C_6H_5)_2COH.COOH$$

In a 500-cc. round-bottomed flask, fitted with a reflux condenser, place 20 g. of benzil, 55 cc. of alcohol, 20 g. of solid potassium hydroxide, and 40 cc. of water. Reflux on the water bath for 15

minutes, then pour the mixture into an evaporating dish and allow to stand overnight. On a subsequent day filter the mixture and wash the product of potassium benzilate with a little alcohol.

Dissolve the potassium benzilate in the minimum quantity of warm water and filter, using decolorizing carbon if the solution is turbid and discolored. Acidify the clear filtrate with concentrated hydrochloric acid, isolate the resulting benzilic acid, and recrystallize all or part from water if purification seems desirable. Yield, 12 g. Melting point of pure benzilic acid, 150°.

343. Perkin Synthesis. This reaction illustrates the ability of an aromatic aldehyde to react with a carbon atom holding at least one reactive hydrogen atom. Usually this carbon-hydrogen group exhibits such reactivity because it is adjacent to a carbonyl group. Acetic anhydride conveniently furnishes such a structural system. A three-carbon-atom side chain is thus established on the benzene ring, leading in the present example to cinnamic acid.

This experiment requires an alkali acetate as an auxiliary reagent, and potassium acetate seems to be more efficient than the sodium salt formerly recommended. In the present directions the potassium acetate is synthesized in the procedure itself. Pyridine has been recommended as a catalyst, and it is suggested that students test its value by adding a few drops to the original reaction mixture.

$$C_6H_5CHO + CH_3CO.O.COCH_3(+ K_2CO_3 \text{ or } CH_3COOK) \rightarrow$$
$$C_6H_5CH = CH.COOK$$
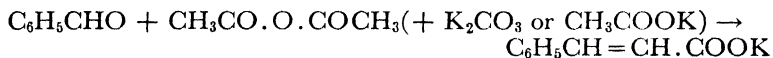
which upon acidification gives cinnamic acid,

$$C_6H_5CH = CH.COOH$$

344. Cinnamic Acid. In a dry 200-cc. round-bottomed flask place 10 g. of pure benzaldehyde, 15 g. of freshly distilled acetic anhydride, free from more than traces of acetic acid, and 7 g. of thoroughly dried potassium carbonate. The benzaldehyde should have been washed free of benzoic acid, dried, and distilled before use. Attach an air-cooled reflux condenser, on the top of which is mounted a small calcium chloride tube, and mix the reagents thoroughly by shaking.

Cautiously introduce the flask, with attached condenser, into an oil bath heated to 180°. Foaming will now ensue for 5 minutes or more, caused by escaping carbon dioxide. When the foaming has somewhat abated, heat the reaction mixture steadily for 30 minutes (see note at end of directions) at 180° to 190°. Now cool the flask

to 100° or below, and wash the contents out into a beaker with a solution of 45 cc. of 6N sodium hydroxide in 150 cc. of water. Heat the resulting alkaline mixture until all lumps are disintegrated, cool, and filter to remove possible traces of more or less solidified tarry matter.

Wash the filtrate with 10 to 15 cc. of benzene and decolorize with carbon as described in § 109. To the clarified hot filtrate add an appropriate acid to free the cinnamic acid. If slow crystallization and larger crystals are desired, use 25 cc. of glacial acetic acid and wrap the vessel with a towel. Otherwise use 30 cc. of conc. hydrochloric acid. After crystallization seems to be nearly complete, cool the mixtures in an ice bath, filter, and wash the product with ice water. The cinnamic acid may be recrystallized from boiling water. Melting point, 133°, yield, 6 to 7 g.

Note. Experiments in which the time of the main reaction was cut below 30 minutes gave low yields. It is questionable, however, whether the long periods usually specified for this operation (3 to 8 hours) give sufficient additional yield to be worth while. Students are invited to test this point further and report to the instructor.

EXPERIMENT 43

Quinone (Benzoquinone)

Hydroquinone + bromate ion + H⁺ →
Quinone + bromide ion + H_2O
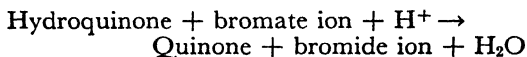
345. The oxidation of hydroquinone (*p*-dihydroxybenzene), while not economical industrially, is the most convenient reaction for preparation of small quantities of quinone in the laboratory. Apparently it is necessary to have an oxidizing agent of moderate activity, present in a solution of carefully adjusted acidity (Method of McCoy, 1937).

In a 200- or 250-cc. flask place 10 g. of hydroquinone, 5.5 g. of potassium bromate, 5 cc. of N sulfuric acid, and 100 cc. of water. Slowly heat the mixture to 60°. The solids dissolve, and the reaction starts promptly. Soon the greenish-black crystalline quinhydrone appears, indicating that part of the material has been oxidized. Without further heating, the temperature rises spontaneously to about 75°.

After about 15 minutes the oxidation is complete, as indicated by a change in color to the bright yellow of quinone. Now heat the mixture to 80° to dissolve the quinone completely, and finally cool it in an ice bath to 0°. Collect the crystalline quinone on a filter, wash with ice water to eliminate salts, and dry. Yield, 8 g.; m. pt., 115.7°. Note that quinone has an appreciable vapor pressure in the solid state, and has a mildly offensive pungent odor.

346. Quinhydrone. Quinone and hydroquinone combine instantly, mole for mole, at ordinary temperatures to form the addition compound quinhydrone $(O=C_6H_4=O$........$HOC_6H_4OH)$. This substance is a valuable reagent in potentiometric analysis.

Dissolve 0.5 g. of hydroquinone in 30 cc. of lukewarm water (30° to 40°) in a small beaker or flask. Into this solution pour with stirring a solution of 0.5 g. of quinone (approximately an equimolal quantity) in 8 to 10 cc. of ethyl alcohol. Allow to stand in a cool

place without further agitation. Shiny, greenish-black crystals of quinhydrone separate. Collect on a filter, wash rapidly with a little cold water, and dry. Do not attempt to recrystallize, as partial decomposition, difficult to detect, may occur.

If one wishes to prepare quinhydrone in quantity with economy of effort, it is best to add to a solution of commercial hydroquinone just half of the amount of a suitable mild oxidizing agent (ferric ion) theoretically required to produce quinone. Quinhydrone then crystallizes directly. The method of preparation, including the problem of impurities, is discussed by W. Mansfield Clark, *The Determination of Hydrogen Ions*, 3d. ed., p. 410, Williams and Wilkins, 1928.

OPTIONAL EXPERIMENTS

347. Anthraquinone. The preparation of purified anthracene obtained in § 198 is suitable for use in a reaction of direct oxidation. Chromic acid attacks the two most central hydrogen atoms, numbered as 9 and 10, replacing them with oxygen. The resulting derivative, anthraquinone, is thus structurally two benzene rings connected by two ketone groups, $C_6H_4(-CO-)_2C_6H_4$.
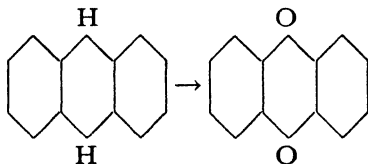
In a small flask equipped with a reflux condenser place 2 g. of purified anthracene and 20 cc. of glacial acetic acid. Dissolve 3 g. of chromic anhydride in a mixture of 10 cc. of glacial acetic acid and 10 cc. of water. See § 348 for method of preparing the anhydride.

Heat the anthracene mixture to boiling, and slowly add the chromic solution through the top of the condenser. (If the preparation is attempted on a large scale, a two-necked flask and dropping funnel should be provided.)

Boil the reaction mixture for 10 minutes and filter by suction. The solid residue is crude anthraquinone. Wash it with water, dry on a steam bath, in an oven, or in the open air, and sublime in a manner similar to that employed with anthracene. It is preferable to use a smaller beaker in which to vaporize the anthraquinone.

348. Preparation of Chromic Anhydride. Dissolve 6 g. of sodium dichromate (dihydrate) in 15 cc. of water. To this solution add 25 cc. of concentrated sulfuric acid in a fine stream, with stirring. Cool the mixture to room temperature to permit adequate crystallization. Mount a common conical funnel in a suction flask, and place in the funnel a piece of glass wool just large enough to block the passage into the stem. Quickly pour out the chromic anhydride mixture upon this funnel, and suck down as much mother liquor as possible. No washing should be attempted.

Without further treatment the crystalline mass of chromic anhydride is used in the oxidation of anthracene. If the work is done carefully the yield will be greater than 3 g., but the excess will do no harm, and the whole product may be used as described above.

Questions

1. Why would you expect the central hydrogen atoms of anthracene to be removed rather than some of the outer ones?

2. Draw a vapor-pressure curve for anthracene based on your observation of its behavior in the laboratory during the process of sublimation.

3. What becomes of the chromic anhydride?

4. Why was glacial acetic acid employed?

EXPERIMENT 44

Wurtz Reaction

349. The reaction of an alkyl halide with metallic sodium normally causes the formation of a paraffin hydrocarbon by the combination of alkyl radicals, with elimination of a sodium halide as a byproduct.

$$2RBr + 2Na \rightarrow R-R + 2NaBr$$
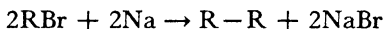
350. n-Octane. Purified n-butyl bromide is prepared by washing a crude technical or student preparation successively with 70% sulfuric acid, dilute sodium hydroxide, and water, and drying the product over calcium chloride or magnesium sulfate.

Mount an outfit as pictured in § 24 with loose clamp adjustment to permit shaking by hand. Place in the flask 14 g. of clean sodium metal cut into 3-mm. cubes. Add slowly 50 cc. of the purified n-butyl bromide with occasional shaking of the flask, using an ice bath if the reaction becomes too vigorous. Heat the completed mixture in a water or oil bath at 100° for 1 hour, distil from an oil bath, and provide for safe disposal of the waste sodium (CARE!) as described below in § 351.

The crude n-octane is now refluxed with additional clean sodium until no test for bromide (§ 420) is obtained. Wash the preparation successively with dilute sulfuric acid, conc. sulfuric acid, water, dilute sodium carbonate or hydroxide, and water. Dry over magnesium sulfate and distil. Yield, 15 g. Boiling point of n-octane 125.5°.

351. Disposal of Waste Sodium. Any solid residues which might possibly contain metallic sodium should be treated with 95% alcohol until the metal has disappeared. It is best to add the sodium residues to excess of alcohol. Never throw sodium wastes into sinks or water! This imperative warning calls attention to the fact that the explosions which come from contact of sodium with

water are not merely hydrogen-oxygen reactions like those often witnessed in elementary laboratories. To be sure, the spontaneous ignition of sodium in contact with water, hydrogen, and air will initiate what would ordinarily be a mild hydrogen explosion. This preliminary explosion then breaks up the residue of hot, liquid sodium and scatters it as a spray in the surrounding atmosphere, where the metal evaporates, mixes with atmospheric oxygen, and detonates with violence. The whole procedure occurs in a minute fraction of a second and is somewhat analogous to the explosion of common gasoline in an automobile motor, where the carburetor spray operation, followed by a mild preliminary explosion of the gaseous pentane fraction, helps to "atomize" the heavier, less volatile hydrocarbons, and to cause them to mix rapidly with oxygen.

EXPERIMENT 45

The Wurtz-Fittig Reaction

352. When an alkyl halide, aryl halide, and metallic sodium are all mixed together one might expect considerable yields of three hydrocarbons. Apparently the mechanism by which a dialkyl or diaryl hydrocarbon would be formed involves at least one slow step. Accordingly the union of alkyl and aryl radicals, not so retarded, is accomplished with satisfactory yield.

353. n-Butylbenzene. Place 75 cc. of purified dry ether (as described in § 357) in the flask of an outfit as pictured in § 355, and extrude into the ether 11.5 g. of sodium wire or ribbon from a sodium press. Surround the flask with an ice bath, and add slowly from the funnel a mixture of 30 g. of pure, dry, n-butyl bromide (see § 222) and 30 g. of pure dry bromobenzene, shaking at intervals but avoiding refluxing. Allow the mixture to stand for 24 hours.

Next day add just enough 95% alcohol to dispose of the excess metallic sodium. Cool to 20° or below, filter, wash the salts on the filter with common ether, and add the washings to the filtrate. Now distil out the alcohol and ether from the filtrate. Wash the liquid residue twice with water to remove sodium hydroxide and any other inorganic material, adding a little ether to facilitate separation of phases. Dry the resulting ethereal solution of n-butyl benzene over anhydrous magnesium sulfate, expel the ether, and distil the product (178° to 183°). Yield, 15 g.

Experienced workers preparing this compound in quantity may avoid the use of 95% alcohol introduced above for safety. (See Ref. No. 24.)

EXPERIMENT 46

Grignard Reaction

354. The reaction of an alkyl or aryl halide with metallic magnesium, in the presence of a very weakly basic solvent such as ether, normally produces the corresponding alkyl or aryl magnesium halide, RMgX. In illustrations given herewith, the compound RMgBr, or "Grignard reagent," reacts with a ketone or ester to give a tertiary alcohol.

$$\text{R—Br} \rightarrow \text{RMgBr} \rightarrow \text{R—}\underset{\underset{\text{OMgBr}}{|}}{\overset{\overset{\text{R}'}{|}}{\text{C}}}\text{—R}' \rightarrow \text{R—}\underset{\underset{\text{OH}}{|}}{\overset{\overset{\text{R}'}{|}}{\text{C}}}\text{—R}'$$
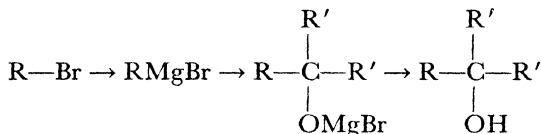
The above representation applies primarily to the use of a ketone. With an ester the formulation is slightly more complex, but in the first experiment described below the product is somewhat easier to purify than that from the ketone.

355. Triphenyl Carbinol. For this experiment the simple arrangement of apparatus shown in the figure is satisfactory. In more troublesome Grignard syntheses mechanical stirring is desirable, leading to the use of the outfit with mercury-sealed stirrer, as shown in § 360. If the Y-tube shown at left is not available, mount the dropping funnel in the top of the condenser, using for this connection a slotted cork which will provide necessary relief of pressure from an otherwise closed system. See that the entire apparatus, including corks, is thoroughly dry before the synthesis is attempted. Provide an ice bath and a supply of anhydrous di-

ethyl ether. (See § 357.) Do not interrupt the experiment from this point until the Grignard complex has been disintegrated with the aid of dilute sulfuric acid as described below.
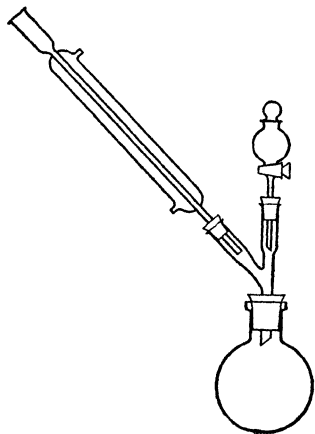
Place in the flask 0.16 gram-atom (3.9 g.) of freshly cut magnesium turnings; the pure metal is desirable, though in wartime turnings of Dowmetal alloy have been used with fair results, involving slight discoloration of both reaction mixture and product. Add a small crystal of iodine and about 15 cc. of anhydrous ether. Now weigh out 0.17 mole of dry bromobenzene, and add through the dropping funnel about 4 cc. of this halide. With a water bath heat the reaction mixture to the boiling point. The reaction should now start, as evidenced by bubbling of the liquid without aid of external heat and by development of a gray, muddy appearance in the solution. If it does not start readily, it is likely that the system is not thoroughly water-free, or the magnesium metal is corroded. Should the trouble be not serious, the reaction may often be encouraged to start by rubbing a fragment of magnesium with the end of a dry stirring rod beneath the surface of the reaction mixture.

As soon as the reaction starts, add 70 cc. more of anhydrous ether. Now through the funnel add the rest of the bromobenzene at a rate slow enough so that the condenser can readily take care of the expelled ether. Reflux the final completed mixture for 30 minutes.

Dissolve 0.08 mole of ethyl benzoate in 35 cc. of anhydrous ether. Allow this solution to drop gradually into the Grignard reagent in a manner similar to the addition of the bromobenzene. Before starting the hydrolysis, be sure that the slightly viscous reaction product is thoroughly mixed. After allowing the mixture to stand for 30 minutes, pour it into a flask in which have been placed 100 g. of ice, 150 cc. of water, and 10 or 12 g. of conc. sulfuric acid. Stir so that the Grignard complex will be completely disintegrated, and the resulting triphenyl carbinol dissolved in the ether. Add more (ordinary) ether if necessary to dissolve the product. Separate the ethereal solution and wash with two 25-cc. portions of 2 to 3N sulfuric acid.

Set up the standard outfit for steam distillation (§ 43), and place the ethereal solution of crude triphenyl carbinol in the main flask. With the aid of a water bath distil the ether, preserving the recovered ether distillate, and then pass steam through the residue to carry out any volatile residues or products. Recrystallize the solid

product from ethyl alcohol under reflux condenser. (See § 101.) Yield, 10 g. Melting point of pure triphenyl carbinol, 162°.

Substitution of other halides for the bromobenzene specified above may be made, but should not be made indiscriminately. Many Grignard reagents do not behave in the conventional manner, and side reactions prevail. (See *J. Org. Chem.*, **1**, 209 (1936).)

356. n-Butyl Dimethyl Carbinol. Synthesis of this compound involves the preparation of a *n*-butyl Grignard reagent, which is accomplished somewhat more readily than the formation of the phenyl derivative. The phenyl bromide and ethyl benzoate of § 355 are replaced by *n*-butyl bromide and acetone, the latter especially well dried with freshly prepared anhydrous magnesium sulfate. Use chemically equivalent amounts of magnesium and acetone, and a 25% excess of butyl bromide.

After the preparation of butyl magnesium bromide, reaction with acetone, and hydrolysis with dilute sulfuric acid, dry the resulting ethereal solution of crude *n*-butyl dimethyl carbinol with anhydrous magnesium sulfate or potassium carbonate, and distil fractionally from an ordinary distilling flask to eliminate the ether. Yield, about 50%. Boiling point of *n*-butyl dimethyl carbinol, 142°. Further details as to behavior of Grignard reactions of this type are described by Fisher (Ref. 33).

357. Anhydrous Ether. On account of fire hazard and losses by evaporation involved in purification of technical ether, it is desirable to use commercial, so-called anhydrous, ether, which is practically free from alcohol and nearly water-free. A small amount (1 to 2 g. per 100 cc. of ether) of metallic sodium wire or ribbon is extruded from a sodium press directly into the bottle of ether, and the bottle is corked only moderately tightly so that traces of hydrogen may escape without developing pressure. When production of bubbles on the surface of the sodium ceases, the solvent is ready for a Grignard synthesis. See § 351 for discussion of danger in final disposal of the sodium waste.

   If only common technical ether is available, it should first be freed from alcohol and most of its water content as follows. Wash 200 cc. of ether with two 15-cc. portions of cold water and three 25-cc. portions of saturated calcium chloride solution. Now add about 15 g. of granular anhydrous calcium chloride and set aside

for a day or more in a well-stoppered vessel.   Finally remove the calcium chloride and give the residual ether the treatment with sodium wire described in the first paragraph of this section.   A few hours over sodium should conclude the process.

In laboratories where the sodium treatment is not favored because of fire and explosion hazard, treat the ether, from which the solid calcium chloride has just been removed, with 10 or 12 g. of phosphorus pentoxide, which is rapidly handled.   Mix well and distil into a dry receiver protected as shown in Fig. 1, § 33.

Optional Syntheses

358. Triphenyl carbinol may also be prepared from benzophenone. Use the above directions, substituting 0.16 mole of benzophenone for the 0.08 mole of ethyl benzoate called for above.   Additional ether may also be required to dissolve the benzophenone.

Acids may be prepared by introducing solid carbon dioxide ("Dry-Ice") into a Grignard reagent (Refs. 25, 31).

Questions

1. What undesired reaction would take place if water were admitted early in the experiment?

2. What chemical principle would lead you to expect such a reaction with water?

3. Why is there no concern about entrance of water after the ethyl benzoate has been added?

4. Why is alcohol removed from commercial ether before use in a Grignard reaction?

5. Represent structurally the preparation of the following by Grignard syntheses: (a) 3-pentanol, (b) phenylacetic acid, (c) β-phenylethyl alcohol, (d) p-tolyldiphenyl carbinol.

EXPERIMENT 47

Malonic Ester Synthesis

359. Although diethyl malonate contains no free acidic carboxyl groups, the compound is still an acid by virtue of the reactivity of the hydrogen atoms attached to the central carbon atom. It may therefore be converted into a sodium salt either by the use of metallic sodium, which by itself is mechanically undesirable, or of the sodium salt of an acid much weaker than malonic ester, such as ethyl alcohol.

If an appropriate halide like benzyl chloride or *n*-butyl bromide is now introduced, the new organic radical—benzyl or butyl—becomes attached to the central carbon atom, with formation of sodium halide as a by-product. By hydrolysis and loss of carbon dioxide the resulting complex substance is cut down to a simple carboxylic acid in which the original radical (benzyl, butyl, etc.) is found attached to the residue $-CH_2 . COOH$:

$$C_2H_5-O-\underset{O}{\underset{\|}{C}}-\underset{H}{\overset{H}{\underset{|}{C}}}-\underset{O}{\underset{\|}{C}}-O-C_2H_5 + C_2H_5ONa \rightarrow C_7H_{11}O_4Na, \text{ the monosodium salt.}$$

$$\text{Addition of } \ \ \bigcirc\text{CH}_2\text{Cl} \ \rightarrow$$

$$C_2H_5-O-\underset{O}{\underset{\|}{C}}-\underset{\underset{\bigcirc}{CH_2}}{\overset{H}{\underset{|}{C}}}-\underset{O}{\underset{\|}{C}}-O-C_2H_5 + NaCl$$

$$\text{Hydrolysis} \rightarrow HOOC-\underset{\underset{\bigcirc}{CH_2}}{\overset{H}{\underset{|}{C}}}-COOH$$

$$\text{Decomposition} \rightarrow \begin{array}{c} \bigcirc \end{array} \begin{array}{c} CH_2.CH_2.COOH \\ \end{array} + CO_2$$
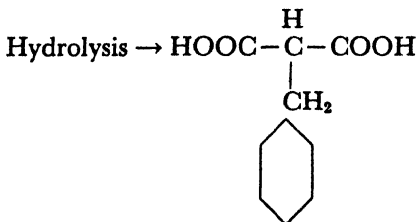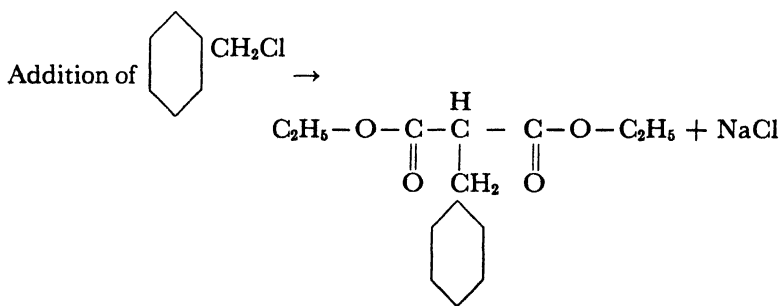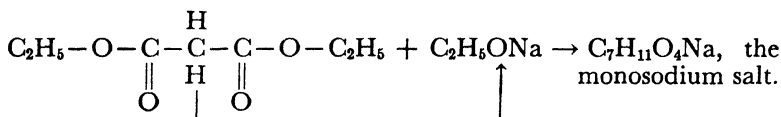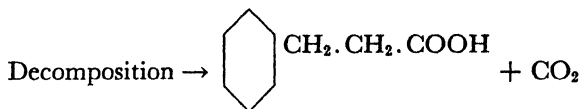
The intermediate designated above·as "monosodium salt" has been represented by different structural formulas in various texts. Probably the true structure cannot be represented by any one fixed formula of conventional design, but rather illustrates the concept of resonance.

360. Hydrocinnamic Acid. In the apparatus with mercury-sealed stirrer shown in the accompanying figure place 250 cc. of absolute alcohol, which must be as nearly anhydrous as possible; preferably not below 99.9% and under no circumstances below 99.8. (See § 361.) (If such apparatus is not available, a simple flask with reflux condenser may be used, with slight disadvantage on account of occasional necessity for shaking by hand.)

Gradually introduce through the condenser 11.5 g. of clean metallic sodium which has been cut into 15 or 20 fragments. After the sodium has all reacted, add with stirring 78 cc. of purified diethyl malonate (same as "ethyl malonate"), which has been redistilled under reduced pressure if necessary. Now run in very slowly with stirring 58 cc. of freshly distilled benzyl chloride. Reflux the mixture, with stirring, for 4 hours, during which time a quantity of sodium chloride is precipitated.
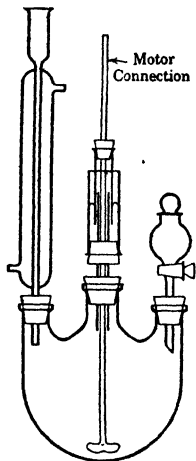
Rearrange the condenser for ordinary distillation, and distil as much of the remaining ethyl alcohol as possible from a steam bath. To the residue add 200 cc. of water and separate the oily layer of crude benzylmalonic ester. Now place this ester in a 500-cc. round-bottomed flask containing a solution of 75 g. of potassium hydroxide in 75 cc. of water. Reflux this mixture until hydrolysis is complete (about 2 hours), and then remove residual alcohol by distillation. Wash the resulting aqueous solution of potassium benzylmalonate with a small amount of ether to remove impure, unhydrolyzed oily matter, adding a little water if necessary to dissolve any solid salts present.

Heat the clear potassium benzylmalonate solution to about 80° and slowly add through the reflux condenser 175 cc. of 10N sulfuric or hydrochloric acid. After foaming has ceased, reflux the mixture for 3 hours. Cool, add water to dissolve any precipitated salt, then extract the oil with ether. Dry the ethereal solution over anhydrous magnesium sulfate, remove the ether, and distil the residue under reduced pressure, preserving the fraction boiling from 164° to 172° at 25 mm.

The product will slowly crystallize at room temperatures. Recrystallization from petroleum ether, with final cooling to 0°, is more rapid. Yield, 20 g. Melting point of pure hydrocinnamic acid, 48.5°.

When *n*-butyl bromide is used instead of the benzyl chloride, a liquid product, *n*-caproic acid, is obtained (Refs. 23, 24).

Questions

1. Why is it not satisfactory to use the simple method of replacing hydrogen in malonic ester directly with metallic sodium, instead of expending necessary time and material in providing of absolute alcohol?

2. Why must the alcohol be so nearly pure?

3. How could dibenzylacetic acid be prepared, using the malonic ester synthesis?

4. In the synthesis suggested in question 3, why is it not possible to introduce two benzyl groups in one alkylation operation?

361. Extremely Dry Ethyl Alcohol. There is often a need (*cf.* §§ 360, 363) for alcohol of less than 0.25% water content. Commercial "absolute" alcohol, or the product from the experiment of § 213, is usually not up to this standard of dehydration after storage. Advantage is then taken of the rapid method of drying by alkaline hydrolysis. Alcohol of any grade above 99% is suitable.

Ethyl formate and sodium ethoxide are allowed to react with the water in the alcohol. The ester is used in about 25% excess to ensure completeness of dehydration, and the sodium ethoxide in about 50% excess to ensure final destruction of the volatile ester. The following is an outline indicating substances used and formed in the three stages of the process.

$C_2H_5OH + H_2O + Na \rightarrow NaOC_2H_5 + NaOH + H_2 (+ \text{ residual } H_2O)$

$H_2O + NaOC_2H_5 + HCOOC_2H_5 \rightarrow HCOONa + C_2H_5OH$

Excess $HCOOC_2H_5$ (in presence of $NaOC_2H_5$) $\rightarrow CO + C_2H_5OH$
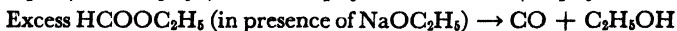
The resulting alcohol, distilled in dry apparatus, will be so close to 100%

that the figure for water content will be below the limit of experimental error in the paraffin oil test of § 215. Workers wishing to test this method to the limit of efficiency should arrange apparatus permitting a change from reflux to distillation without breaking connection between condenser and flask. (Modification of method of Adickes, *C.A.*, **25,** 1796 (1931).)

In a 1-l. round-bottomed flask fitted with a reflux condenser place 300 cc. of alcohol (99% or better), and add 2 g. of metallic sodium, in slices, for each 1 g. of water present in the alcohol. When the sodium has completely reacted, add 3 cc. of ethyl formate for each 1 g. of sodium used. Within a few seconds sodium formate, almost insoluble in anhydrous alcohol, is precipitated.

Reflux the mixture on the water bath for 30 minutes. Dehydration is complete for all practical purposes in less than 5 minutes; but the catalyzed disintegration of residual ethyl formate and expulsion of carbon monoxide is somewhat slower.

Distil the reaction mixture with precautions to exclude moisture. Set aside the first 20 cc. and collect the next 200 or 250 cc. for immediate use in the special experiment requiring the dry solvent (such as § 360 or § 363). Finally wash the residue of sodium ethoxide and hydroxide out of the flask as promptly as possible, since this strongly alkaline material attacks glass.

EXPERIMENT 48

Acetoacetic Ester Synthesis

362. Like malonic ester, ethyl acetoacetate, or acetoacetic ester, contains reactive hydrogen attached to a carbon atom which in turn is adjacent to carbonyl groups on both sides. Accordingly, it may be converted into an alkylated derivative by a procedure much like that described in § 359. Hydrolysis of this derivative—with proper attention to alkali concentration—yields a ketone instead of the acid obtained in § 360.

$$CH_3CO . CH_2COOC_2H_5 \rightarrow \text{monosodium salt}$$

Monosodium salt $+ C_4H_9Br \rightarrow CH_3CO . CH(C_4H_9) . COOC_2H_5$.
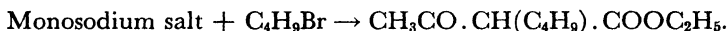
Hydrolysis and loss of CO_2 cause the formation of a ketone;

$$CH_3CO . CH_2 . C_4H_9.$$

Other modifications of the acetoacetic ester synthesis are described in advanced texts.

363. Methyl *n*-Amyl Ketone. Either a simple round-bottomed flask with reflux condenser or the outfit with mercury-sealed stirrer pictured in § 360 may be used. The condenser should be protected with a calcium chloride tube. Read these directions through and decide on the basis of available time which of the alternative methods and arrangements of apparatus is preferable. Do not interrupt this experiment until the butyl bromide has been added.

Place 200 cc. of extremely dry "absolute" alcohol (not under 99.8%—see § 361) in the flask under reflux condenser, and add 9 g. of clean sodium, cut into small fragments, as fast as possible without causing excessive ebullition. To the resulting warm solution of sodium ethoxide add gradually with shaking or stirring, according to apparatus used, 48 g. of pure ethyl acetoacetate. Now add rapidly 55 g. of pure *n*-butyl bromide with shaking or stirring, and reflux the mixture for 5 hours or more.

Rearrange the apparatus for ordinary distillation and distil out the alcohol. Cool the residual liquid to room temperature, and

wash with a solution of 3 to 5 cc. of conc. hydrochloric acid in about 300 cc. of water, to dissolve and remove sodium bromide. The residual oil is mixed with 350 cc. of 5% sodium hydroxide solution. The following alternative procedures are now appropriate: either shake in a stoppered bottle for 30 minutes and let stand until the same laboratory period next day, but not longer, or stir vigorously under reflux, with mechanical stirrer, for 4 hours. At the end of the chosen period of reaction remove any unhydrolyzed oily matter and place the aqueous residue in a distilling flask equipped as shown in Fig. 4, § 33.

Add slowly a solution of 20 cc. of conc. sulfuric acid in 40 cc. of water. After most of the carbon dioxide has escaped, distil until about half of the liquid has passed over. Make the distillate alkaline with solid sodium hydroxide, and redistil until 80 to 90% of the distillate has again passed over.

Separate the ketone layer and redistil the aqueous layer until about half has passed over. Separate the small additional yield of ketone and combine it with the main product. Extract the water layer of the final distillate with 25 to 30 cc. of ether, and add the ether extract to the ketone product. Wash the combined ketone extract twice with half its volume of saturated calcium chloride solution, dry over magnesium sulfate (5 g.), and distil. Collect the fraction boiling at 145° to 152°. Yield, 15 to 20 g.

Questions

1. Using the same reagents, represent structurally the procedure by which you would prepare a substituted acetic acid instead of methyl amyl ketone.

2. Explain how a sharp deviation from Raoult's law permits the peculiar technique of distillation described in the last paragraph, whereby a relatively less volatile product comes over rapidly.

EXPERIMENT 49

Friedel-Crafts Synthesis

364. When benzene or other suitable aromatic compound con-
taining no interfering groups is treated with an alkyl or acyl halide,
or an acid anhydride, in the presence of anhydrous aluminum
chloride, the alkyl or acyl radical, as the case may be, may replace
hydrogen on the aromatic nucleus. For example, benzyl chloride is
converted into benzyl benzene, or diphenylmethane.

$$C_6H_6 + C_6H_5CH_2Cl(+ AlCl_3) \rightarrow C_6H_5CH_2C_6H_5 + HCl$$

365. Diphenylmethane. A 500-cc. round-bottomed flask under
reflux condenser is arranged so that the gaseous hydrogen chloride
by-product may be caught in alkali solution as shown in the illustra-
tion of § 367. It is convenient to incorporate an addition tube in the
apparatus, with a final assembly which would be virtually a com-
bination of features shown in § 355 and § 367.

Place in the flask 120 cc. of dry, thiophene-free benzene, which
has been purified if necessary by agitation with concentrated sul-
furic acid, washing, and drying. Add 34 cc. of dry redistilled benzyl
chloride, and provide 11 g. of anhydrous aluminum chloride in a
dry test tube. (If a new unopened bottle of commercial aluminum
chloride is provided, consult the instructor or storekeeper about
danger from gas pressure in the sealed bottle.)

Keeping the reaction mixture continuously cool with the aid of an
ice bath, add the aluminum chloride in several portions, waiting
after each addition until the initial vigor of the reaction subsides.
Reflux the final mixture on the water for 30 minutes, allow to cool
and add about 100 g. of ice. Separate and preserve the upper or
benzene layer.

Remove the benzene (and simultaneously the water) from the re-
action mixture by ordinary distillation from an oil bath at 110° to
120°. Transfer the resulting crude diphenylmethane to a Claisen
flask. Distil under reduced pressure, first eliminating the small

residue of benzene and resuming distillation for the main product at 20 to 30 mm. Yield, 25 g. Boiling point of pure diphenylmethane at 760 mm., 262°; at 22 mm., 145°. Melting point, 27°.

Optional Syntheses

366. Benzophenone. Benzoyl chloride is condensed with benzene, yielding a ketone instead of a hydrocarbon (Refs. 8, 16, 25, 27, 30, 31, 32, 34, 35, 39, 41, 43).

Acetophenone. (Refs. 23, 24, 25, 27, 28, 30, 35, 37, 38, 40, 41, 45.)

o-Benzoylbenzoic Acid. An acid anhydride is condensed with benzene (Refs. 12, 25, 30, 31, 33, 37, 40).

EXPERIMENT 50

Nitriles and Cyanohydrins

367. The cyanide group may be attached to carbon by the reaction of an alkyl halide with sodium cyanide, yielding a nitrile:

$$RCl + NaCN \rightarrow RCN + NaCl$$
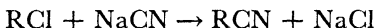
If an aldehyde or ketone is substituted for the halide, hydrogen cyanide is then employed, yielding a cyanohydrin:

$$R.CHO + HCN \rightarrow R.CHOH.CN,$$

or

$$R-\underset{\underset{O}{\|}}{C}-R + HCN \rightarrow R-\underset{\underset{OH}{|}}{\overset{\overset{C\equiv N}{|}}{C}}-R$$
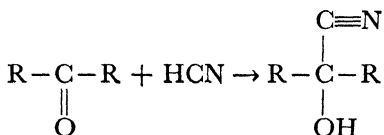
Hydrolysis of each of these products yields an acid (RCOOH. RCHOH.COOH or RC(OH)(COOH)R).

The preparation of a halide suitable for the nitrile synthesis is first described.

$$CH_3.CH_2.COOH + Br_2 \rightarrow CH_3.CHBr.COOH + HBr$$
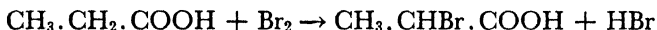
368. α-Bromopropionic Acid. In a 500-cc. round-bottomed flask, as illustrated in the accompanying figure, place 74 g. (1 mole) of freshly distilled propionic acid (b. pt. 139° to 140° uncor.), 1 g. of red phosphorus, and 224 g. (1.4 mole) of bromine which has been dried by shaking with concentrated sulfuric acid in a separatory funnel.

In selecting the rubber stopper which connects the reflux condenser to the flask it is well to choose an old specimen which has slightly hardened and thus has a surface somewhat more resistant to the reactive bromine. The funnel which delivers the by-product of hydrogen bromide gas to the sodium hydroxide solution should be fastened so that it will barely dip beneath the surface of the liquid in the beaker. In the event that the pressure inside the flask should fall, the sodium hydroxide will not be sucked into the condenser.

The reaction mixture is slowly heated on the water bath until hydrogen bromide is freely liberated. Usually the evolution of gas starts at a temperature between 50° and 60°. The heating is then gradually increased until all bromine seems to have reacted with the propionic acid. The time may vary from 4 to 8 hours according to the rate of heating. The mixture is now transferred to a 250-cc. Claisen flask and distilled under reduced pressure with the aid of a filter pump. The fraction boiling at 105° to 109° at 27 mm. pressure is collected. Yield, 85 to 90% of the theoretical.
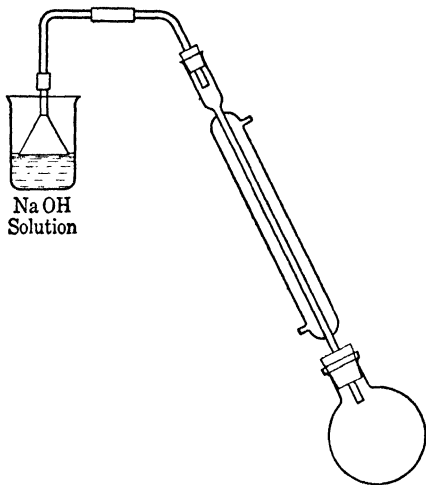
Optional Synthesis

369. Benzyl Chloride. If commercial cylinder chlorine is available, benzyl chloride may be prepared by the chlorination of boiling toluene (Refs. 26, 27, 28, 30, 32, 35, 40, 43).

370. Methylmalonic Acid. In a 2-l. round-bottomed flask place 153 g. (1 mole) of α-bromopropionic acid. To this add a 25% solution of sodium carbonate until the solution is alkaline to phenolphthalein. For this purpose dissolve 60 g. of the anhydrous carbonate in 180 cc. of water. If this amount is insufficient, add 6N sodium hydroxide, a few cubic centimeters at a time, until the alkaline reaction is obtained. A supply of crushed ice should now be provided, also means for cooling the 2-l. flask under the tap.

Now add a solution of 53 g. (1 mole) of 95% sodium cyanide in 150 cc. of warm water and heat the resulting mixture to 50° or 60°. The reaction which now sets in is likely to be so vigorous that the flask will have to be cooled under the tap. If such water cooling is insufficient to control the reaction, add a few pieces of ice to the reaction mixture. When the temperature no longer tends to rise

spontaneously, heat the mixture in a boiling water bath for 45 minutes. An excess (80 g.) of commercial solid sodium hydroxide is now added slowly, and the mixture is boiled on an oil bath until all ammonia has been expelled. The passage of a slow current of air through the solution expedites the removal of ammonia.

When only traces of ammonia remain, cool the liquid to 20°. Add cautiously, with continued cooling, an excess (300 cc.) of commercial conc. hydrochloric acid. (**Warning.** Some *hydrogen cyanide* may be liberated at this stage; accordingly perform this part of the experiment out of doors or in a hood.)

Now add to the mixture 160 g. of hydrated sodium sulfate ($Na_2SO_4.10H_2O$), cool in ice water, and filter through a Buechner funnel. After the salts on the funnel have been sucked as dry as possible, transfer the filtrate to a large separatory funnel, leaving the salts on the filter. Replace the empty filter flask in position, and wash the salts with 100 cc. of ether. Use this wash ether as the first of six 100-cc. portions of ether which are now to be used, in turn, for six extractions of the aqueous solution in the separatory funnel. (**Warning.** Note precautions described in § 68, dealing with danger in shaking aqueous solutions with ether.)

Dry the combined ether extract over anhydrous magnesium or sodium sulfate, and filter. Distil the ethereal filtrate through a well-cooled condenser. As the rate of accumulation of ether slackens toward the close of the distillation, boil the water in the water bath rapidly to ensure as complete removal of the ether as possible. Now discontinue the heating, and add to the boiler residue 100 cc. of dry benzene.

To the resulting benzene solution gradually add 250 cc. of petroleum ether, "light ligroin," or other light petroleum solvent whose boiling range lies below 120°, and continue the cooling operation. During this process about 80 to 82 g. of nearly white crystalline methylmalonic acid should separate. Collect this on a Buechner filter, and spread upon a porous clay dish to remove water and propionic acid.

Yield (80 g.), 70% of the theoretical.

Questions

1. Why is the bromopropionic acid neutralized before addition of the sodium cyanide?

2. Why is the sodium sulfate added before the solution is extracted?

3. Of what use is the benzene in the recrystallization process?

4. What compound would have been produced if the cyanide had been reduced instead of hydrolyzed?

371. Benzyl Cyanide. Benzyl chloride, used in this experiment, is an offensive substance of lacrimatory type. If it is necessary to distil the reagent, use a hood.

In a 500-cc. round-bottomed flask, fitted with a water-cooled reflux condenser, place a solution of 30 g. of sodium cyanide (poison!) in 35 cc. of warm water, and add 50 cc. of alcohol. Add through the condenser, in several small portions during 10 or 15 minutes, 63 g. of benzyl chloride. Boil the mixture for 3 hours, cool, filter to eliminate the product of sodium chloride, and distil the alcohol from the filtrate. Separate the crude benzyl cyanide, dry for a few minutes over magnesium sulfate, and distil under reduced pressure, 40 mm. being sufficiently low. Yield, 40 g. Boiling point of benzyl cyanide at 40 mm., about 140°; at 760 mm., 232°.

Optional Syntheses

372. Hydrolysis of Benzyl Cyanide; Phenylacetic Acid. The nitrile is hydrolyzed in acid solution, as contrasted with the alkaline hydrolysis of § 370 (Refs. 2, 30, 35, 37, 43).

Partial Hydrolysis; Phenylacetamide. A less drastic treatment leaves nitrogen still attached to the carbon side-chain. (See *Ber.* **18,** 355 (1885).)

n-Butyl Cyanide and n-Valeric Acid. n-Butyl bromide is converted into the nitrile, which in turn is submitted to alkaline hydrolysis (Ref. 23).

Acetonitrile (Methyl Cyanide). This nitrile is commonly made by removal of hydrogen and oxygen (in the ratio of H_2O) from acetamide (Refs. 23, 24, 27, 30, 34, 35, 38, 39, 40, 41, 43, 45).

Benzonitrile. This strictly aromatic nitrile is prepared from a diazo intermediate. (See § 313.)

373. α-Hydroxy-α-Methylbutyric Acid; Cyanohydrin Reaction. Provide 82.5 g. (1.6 moles) of 95% sodium cyanide (poison!), if necessary crushing the commercial product into pieces not more than 1 cm. in diameter. This salt is used in conjunction with a weakly acidic substance as a substitute for the more dangerous free hydrocyanic acid.

In a 3-necked 2-l. flask, equipped with a mechanical stirrer, a dropping funnel, and a long air-cooled condenser, place 200 g. of cracked ice, 25 cc. of water, the 82.5 g. of sodium cyanide, and 108 g. (1.5 moles) of ethyl

methyl ketone. Weigh out 190 g. of sodium metabisulfite, $Na_2S_2O_5$ (equivalent to 2 moles $NaHSO_3$), and dissolve as much as possible of this salt in 240 cc. of hot water (75° to 100°) in a beaker. As the cyanide-ketone mixture is vigorously stirred, introduce from the dropping funnel, during the course of 8 to 10 minutes, the bisulfite solution. By the time that 150 to 175 cc. of the bisulfite solution has been added the temperature should have risen to about 35°. Place a cooling bath of ice and water around the flask, and hold the temperature of the reaction mixture between 30° and 40° for 10 minutes after the last of the bisulfite has been added. After the solution is all in, add the balance of the (solid) sodium metabisulfite directly to the reaction mixture.

The main cyanohydrin reaction should now be complete. Place an ice-salt bath around the reaction flask, and continue the stirring until the temperature of the reaction mixture falls to 0°. Pour the oily cyanohydrin from the mushy salt layer; then add 50 to 100 cc. of water to the latter, and shake thoroughly. Additional oil may rise to the top; if so, pour this off also and place with the first quantity separated. More or less of the aqueous salt solution is likely to flow over with the oil; isolate this in a separatory funnel and discard it, preserving the oil for the hydrolysis reaction next described.

374. Conversion into Acid. The hydrolysis of the cyanohydrin in hydrochloric acid solution requires 7 hours if one must carry on the procedure continuously to the end. Time is saved, on the other hand, by preparing the reaction mixture in the cold, and allowing it to stand for 24 hours or more. When the work is resumed at the next laboratory period, only 4 hours of refluxing are required.

Heat the crude cyanohydrin, of which there should be about 160 g., at 90° to 100°, under a reflux condenser, with 200 g. of conc. hydrochloric acid, and for either the 4 or 7 hours according to the more favored plan of those cited above. It is not advisable to heat the solution above 100°, since both hydrogen chloride and the desired organic product would be lost by volatilization. Now cool the solution to room temperature. Without attempting to remove the ammonium chloride, add 100 g. of hydrated sodium sulfate and shake thoroughly. This operation converts most of the acidic hydrogen into the bisulfate ion (HSO_4^-), and thus markedly reduces the acidity. The sodium sulfate should actually dissolve in order to accomplish its purpose; but it is difficult to determine whether or not the solution is really complete on account of the mass of other salts in suspension. It is well to agitate the solution for about 15 minutes. Now cool the mixture to 10°, and filter with the aid of strong suction, as from an effective filter pump. Reject the residual solid salts, and extract the solution with four 75-cc. portions of ether. Dry the combined extract with 50 g. of magnesium or

sodium sulfate, and distil the ether as completely as possible. Now heat the flask containing the residual product to 100° until no more ether distillate is obtainable. Introduce a capillary tube (as in reduced-pressure distillation, § 36) and cool the flask to room temperature. When the flask is cool, exhaust it to the limit of the filter pump and gradually heat the vessel again to 100°.

To the residue add 25 cc. of benzene and 75 cc. of light petroleum distillate (petroleum ether, or "thinner" solvent with boiling range below 120°); then heat almost to the boiling point of the mixed solvent. Shake the mixture to permit maximum extraction by the solvent, and without cooling immediately decant as much of the clear solution as possible into a second flask, cooled with ice and salt.

After the maximum crystallization of the desired solid acid has taken place, decant as much of the benzene-petroleum mother liquor as possible back into the first flask. Now add another 25 cc. of benzene and 75 cc. of petroleum, and use this new enlarged volume of solvent for the next extraction. Repeat the heating, extraction, and decantation as often as may be necessary to transfer the product and obtain the maximum yield of crystals. Yield, about 64% of the theoretical. The product melts at 72.5° (cor.).

If the product is dark colored or contains foreign matter, dissolve it in the minimum quantity of hot benzene, and filter the solution. Now add two to three volumes of light ligroin (petroleum solvent) and cool in an ice-salt bath.

Optional Syntheses

375. Mandelic Acid. Benzaldehyde is condensed with hydrogen cyanide, yielding mandelonitrile, $C_6H_5.CHOH.CN$. Hydrolysis yields the corresponding (mandelic) acid, $C_6H_5.CHOH.COOH$ (Refs. 24, 26, 27, 31, 34, 35, 40).

Amino-Nitriles. The introduction of ammonia during the reaction of an aldehyde and hydrogen cyanide causes the formation of an a-aminonitrile instead of an a-hydroxynitrile. Hydrolysis of such a product yields an amino acid. *Cf.* aminoacetic acid from formaldehyde (Ref. 4).

EXPERIMENT 51

Triphenylmethane Dyes and Indicators

376. If the para hydrogen on at least two of the three rings of the triphenylmethane molecule is replaced by amine or hydroxyl groups, the resulting derivative is easily transformed into a dye of brilliant color. In the case of crystal violet, three dimethylamino groups are present, one of which is in the ionic or salt form in the final preparation. Care should be taken not to use too little or too much hydrochloric acid, lest there be produced either the free color base or the uncrystallizable di-salt or tri-salt. In the procedure structurally outlined below, the dimethylaniline reacts separately with the ketone (4,4′-tetramethyldiaminobenzophenone), after which the hydrochloric acid is added.

377. Crystal Violet. Select a flask of from 1500 to 2000 cc. capacity which has the necessary accessories for steam distillation later in the process. In this flask place 15 g. of freshly distilled dimethylaniline, 6 g. of Michler's ketone (tetramethyldiaminobenzophenone), and 6 g. of phosphorus oxychloride. Heat the flask in the open for 5 hours on the water bath.

Add about 250 cc. of water and enough sodium hydroxide to render the solution alkaline. Calculate this quantity on the basis

of the hydrolysis products coming from the phosphorus oxychloride. Pass steam through the mixture until all unchanged dimethylaniline has passed over into the receiver. Cool the flask, collect the reddish precipitate of the "color base" upon a Buechner filter, and wash with water. Transfer the precipitate to a clean flask or beaker, and boil it with 250 cc. of water to which just 2 cc. of concentrated (12N C.P.) hydrochloric acid has been added. Filter the hot solution, set the filtrate aside to crystallize, and treat the residue with successive portions of the same water-hydrochloric acid mixture until practically all of the color base has been dissolved.

Saturate the combined filtrates with clean common salt, being careful not to add an excess beyond solubility limits. Allow the mixture to stand a day or more. Collect the resulting crystalline preparation on a filter and dry in the open air. Yield, 8 g.

Optional Syntheses

378. Malachite Green. A dye of structure similar to that of crystal violet, synthesized from benzaldehyde and dimethylaniline (Refs. 24, 27, 28, 30, 32, 34, 35, 39, 40, 43).

Fuchsine (Magenta). Although even simpler in structure than the foregoing dyes, fuchsine is more difficult of preparation (Refs. 28, 30, 43).

Questions

1. In what way is the structure of crystal violet supposed to differ from that of the color base?

2. What happens when the dye is treated with an excess of hydrochloric acid?

3. How may crystal violet serve as an indicator?

4. Why does it have a special usefulness distinct from that of common indicators like litmus, methyl orange, etc.?

5. What is the structure of the leuco form of crystal violet?

379. Phthaleins. When phthalic anhydride is heated with a phenol, a para hydrogen atom from each of two molecules of the latter combines with one of the outer oxygen atoms of the anhydride to form water. The organic residues unite to form a new large molecule, the resulting substance being called a phthalein.

When resorcinol (m-dihydroxybenzene) is used as the phenol, resorcinol phthalein is produced. On account of its fluorescent behavior, the latter has been named fluorescein. In this compound two of the phenolic hydroxyl groups react spontaneously to yield an ether group.

The four hydrogen atoms, ortho to hydroxyl groups, are readily replaced by bromine, yielding tetrabromofluorescein, or eosin, a brilliant red dye used in biological laboratories.

(Fluorescein)

Fluorescein + 4Br₂ →

+ 4HBr

(Eosin)
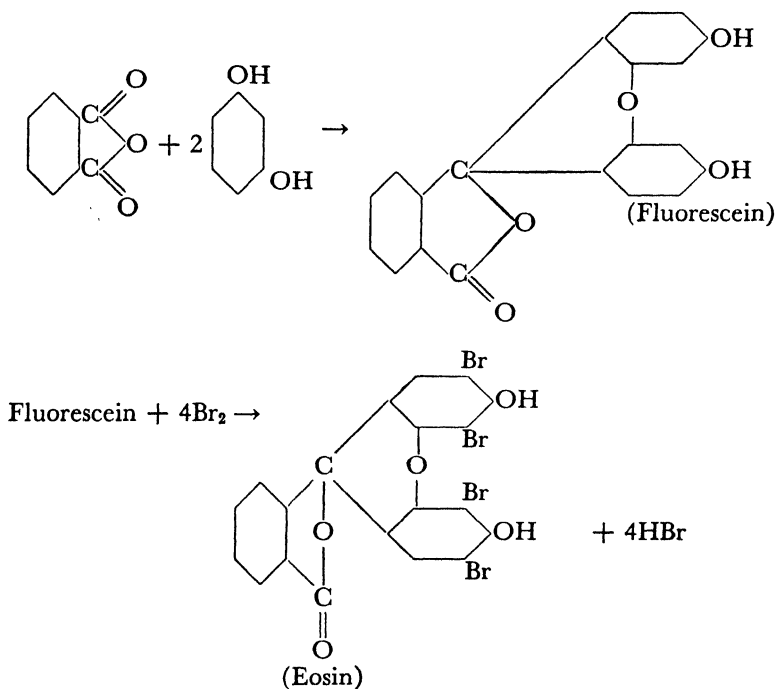
If one of the carboxylic groups in the original phthalic anhydride is replaced with the sulfonic group, a closely analogous derivative may be made. Such a product is known as a sulfonphthalein. Although the mixed carboxylic-sulfonic anhydride, supposedly needed for this synthesis, is not commerically available, it happens that a closely allied substance, benzoic-sulfonic imide (saccharin), serves the purpose.

Saccharin

Phenol Red
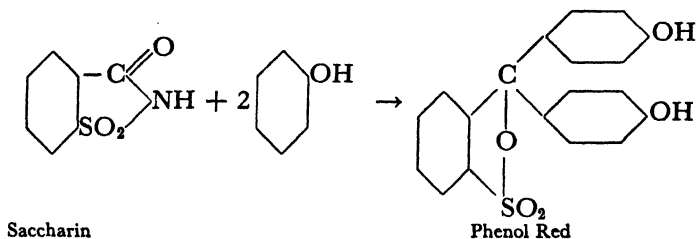
380. Fluorescein. In a conical flask of 300 to 500 cc. capacity place 0.05 mole of phthalic anhydride and 0.1 mole of resorcinol. Suspend the flask in an oil bath and heat the oil to a temperature of about 180°. While the oil is being heated, weigh out rapidly 5 to 7 g. of anhydrous zinc chloride and immediately grind it into a coarse powder in a small mortar. (Note. The zinc chloride must not be exposed to the air longer than is absolutely necessary. If the laboratory supply is obviously wet or hydrated, dry a 10-g. portion by fusing in a porcelain dish.)

As soon as the zinc chloride is ready, stir the powder into the phthalic acid-resorcinol mixture, which by this time has probably melted. Keep the oil at the temperature of 180°, and stir the mixture every few minutes. Excessive heating may permit phthalic anhydride to sublime out of the flask, with resulting loss of yield. The reaction is complete when the solution becomes so viscous that further stirring is not practicable. The dark-red mass consists principally of a mixture of fluorescein with zinc chloride, together with basic zinc salts resulting from partial hydrolysis of the original zinc salt at high temperatures.

Allow the oil to cool to 100°, and add to the reaction mixture 100 cc. of water and 5 cc. of conc. hydrochloric acid. Now raise the temperature of the oil until active boiling of water ensues. Stir the mixture from time to time after the temperature of the oil passes 110°. Careful attention is required at this time to prevent boiling over of the dilute acid. Continue the boiling until the reaction mixture has been disintegrated and all zinc salts dissolved. The insoluble residue, which should be crushed into small pieces, is fluorescein. It is collected on a Buechner filter, washed well with water, and dried in the open air or on a steam bath. Yield, 13 g.

381. Eosin. Take a flask containing 10 g. of fluorescein and 40 cc. of alcohol outdoors or to a hood, and add, drop by drop, 8 cc. of bromine from a dropping funnel. See that the stopcock of the funnel is well lubricated in advance, and be careful not to pull out the plug lest bromine reach the fingers. Should bromine get upon the skin, at once wash with water and follow the suggestions outlined on the inside back cover of this volume.

During the 15 minutes normally required for addition of the bromine, note that the soluble dibromofluorescein first forms. Later the tetrabromide (eosin) is formed. Being only slightly soluble in

alcohol, this substance crystallizes out. After the reaction mixture has stood 2 hours or more, the product is collected on a filter, washed with alcohol, and dried in the open air. Yield, 15 g.

382. Sodium Eosin. Grind together in a mortar 10 g. of eosin and 2 g. of anhydrous sodium carbonate, and place the mixture in a 200-cc. flask or beaker. Add 10 cc. of alcohol and 10 cc. of water, and warm on the water bath until evolution of carbon dioxide ceases. Add 40 cc. of alcohol, heat to boiling, and filter through a fluted filter into a beaker. (A stemless funnel is desirable.) Sodium eosin slowly crystallizes from the filtrate. It may be necessary to aid the process of crystallization by scratching the walls of the beaker with a glass rod.

Other salts of eosin may be prepared in crystalline form. See various manuals of organic chemistry for the preparation of potassium and ammonium eosin; or devise methods of preparing other salts.

383. **Red Ink.** If the faint green fluorescence of eosin is not considered objectionable, an acceptable red writing ink may be made according to the following recipe:

Gum arabic (gum acacia)	2 g.
Water	50 cc.
Thymol	0.2 g.
Sodium eosin	2.5 g.
Aqueous NaOH (N/10)	50 cc.

Soak the gum arabic in the water overnight; or pulverize it, stir rapidly into the water, and mix thoroughly. As soon as the gum is completely dispersed in the water, add the mixture to a second solution, which is prepared in advance by dissolving the thymol, and next the sodium eosin, in the sodium hydroxide solution. Finally filter the completed mixture through a fluted filter, as described in § 99.

The gum aids in permitting the ink to flow in a desirable manner from the pen, while the thymol serves as a preservative and disinfectant. The amount of sodium eosin may of course be varied to suit personal preference.

Optional Syntheses

384. Phenolphthalein requires longer time for preparation than fluorescein (Refs. 27, 28, 30, 40, 41, 43).

Thymolphthalein. Use of thymol instead of phenol gives a beautiful

blue phthalein, useful as a special indicator for pH ranges in the vicinity of 10. (Ref. 25.   See also *Ber.* **28,** 1876 (1895).)

Erythrosine.   The iodination of fluorescein, instead of bromination, yields erythrosine, one of the approved food dyes (*Ind. Eng. Chem.,* **14,** 1115 (1922)).

Mercurochrome.   Dibromofluorescein (*J. Chem. Soc.* **1932,** 724) is mercurated, yielding the well-known brilliantly colored disinfectant mercurochrome (*J. Am. Chem. Soc.* **42,** 2355 (1920)).

Questions

1. In what way does fluorescein differ from phenolphthalein?

2. What change occurs in the structure of a phthalein when it is treated with an alkali?

3. Explain the principle underlying the use of phenolphthalein as an indicator.

4. What is the purpose of the zinc chloride?

385. Sulfonphthaleïns.   When benzoic-*o*-sulfonic imide ("insoluble saccharin") is substituted for simple phthalic anhydride, a series of phthaleins of striking character is developed.   Several of the well-known Clark-Lubs indicators are of this class, including the simplest of the series, which is phenol-sulfonphthalein, or "Phenol Red."

386. Phenol Red.   In a small flask mix 10 g. of insoluble saccharin (the free imide containing no sodium), 25 g. of phenol and 12 cc. of conc. sulfuric acid.   Heat the mixture in an electric oven at 120° for 48 hours.   Dissolve the resulting red, viscous reaction product in 200 cc. of water to which is added enough sodium carbonate to neutralize the acids present.   Steam-distil the solution until excess phenol is expelled, filter, and acidify with hydrochloric acid.

The precipitated Phenol Red may be purified by redissolving in dilute sodium carbonate and reprecipitating with acid.   For further details, see *J. Am. Chem. Soc.,* **50,** 2014 (1928).

EXPERIMENT 52

Derivatives of Nitroparaffins

387. When a 1-nitroparaffin is boiled with aqueous sulfuric acid, the nitro group oxidizes the adjacent methylene group, thus transforming the substance into a hydroxamic acid, which is the N-hydroxylamide of the corresponding aliphatic monocarboxylic acid. Hydrolysis then yields the free aliphatic acid and hydroxylamine sulfate (Method of Lippincott and Hass, 1939).

$$CH_3CH_2CH_2NO_2 + H_2SO_4 + H_2O \rightarrow$$
$$CH_3CH_2COOH + NH_2OH \cdot H_2SO_4$$
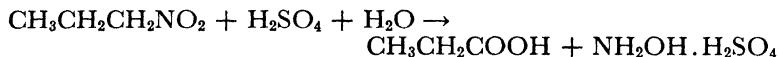
Furthermore, a nitroparaffin molecule may be extended by aldehyde condensation. For example, nitroethane adds two molecules of formaldehyde at the two reactive alpha positions, respectively, yielding a crystalline nitroalkanediol.

$$CH_3CH_2NO_2 + 2HCHO \rightarrow CH_3C(CH_2OH)_2NO_2$$
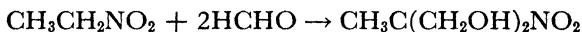
388. Propionic Acid. Equip a 500-cc. three-necked flask with stirrer and condenser as shown in § 360. In place of the dropping funnel use a high-range thermometer with bulb down in the zone of the reaction mixture to be added. Mount the flask so that either a Bunsen flame or cooling bath may be applied as required.

Place in the flask 0.5 mole (45 cc.) of 1-nitropropane and a solution of 30 cc. of conc. sulfuric acid in 5 cc. of water. With the stirrer in operation, heat the mixture to 120°, whereupon the reaction starts, calling for immediate cessation of external heating. The temperature rises to about 128°. If boiling becomes too active, cool the flask slightly with the water bath. When the reaction subsides, renew heating and reflux the mixture slowly for 8 hours on an oil bath. The period of refluxing may be interrupted at the convenience of the operator.

Using a 125-cc. Claisen flask, distil the final two-phase reaction product under reduced pressure (not over 10 mm.) into a 125-cc. common distilling flask, not allowing the temperature of the residue

to rise above 140°. Redistil the distillate of crude propionic acid, collecting the fraction boiling at 137 to 141°. Yield, 20 g. or about 55%. The dark-colored residue may be preserved for use as described in § 389.

389. Acetoxime. The dark-colored residue of crude hydroxylamine acid sulfate may be purified as an inorganic preparation, or may be used to prepare a ketoxime as follows.

Dilute the material with 100 cc. of water, decolorize with carbon, and neutralize (to about pH 7) with sodium hydroxide. Add 0.5 mole of acetone, reflux 1 hour, and allow to stand for a day or more. Extract the resulting acetoxime with ether, dry the ethereal solution over anhydrous magnesium sulfate, expel the ether, and distil the oxime. Boiling point at atmospheric pressure, 136°, m. pt. 60 to 61°.

390. 2-Methyl-2-nitro-1,3-propanediol. In a 250-cc. conical flask place 38 cc. of 40% formalin (commercial aqueous formaldehyde, 0.5 mole) and 2.5 cc. of 1N sodium hydroxide which serves as a catalyst, and provide 18 cc. (0.25 mole) of nitroethane which is to be added from a dropping funnel.

After 3 to 5 cc. of nitroethane has been added dropwise to the flask, with shaking, wait a few moments if necessary until evolution of heat of reaction is evident. Now resume the addition of nitroethane, cooling the flask in a water bath whenever necessary to keep the temperature below 40°. The addition requires 7 or 8 minutes. After the last addition do not cool the mixture, but allow the temperature to rise to 45° or 50°.

Allow the reaction mixture to stand for 1 hour, add 2.5 cc. of 1N sulfuric acid, and see that the solution reacts acid. Cool in an ice bath or place the flask in a refrigerator. Break up the resulting mass of hard crystals and suck dry in a Buechner filter. Yield 23 g., or about 68%. Additional material (about 10 g.) is obtainable by evaporation of the mother liquor to dryness.

EXPERIMENT 53

Cis-Trans Isomerism

MALEIC AND FUMARIC ACIDS

391. Maleic anhydride, an important industrial organic reagent, is readily hydrolyzed to maleic acid, whose molecule, like that of the anhydride, has the "cis" configuration. This product is converted by hydrogen chloride into fumaric acid, its "trans" geometric isomer. According to one theory a molecule of hydrogen chloride undergoes 1–4 addition to the conjugated system, yielding the transitory intermediate represented in brackets below. The hydrogen and chlorine are then presumed to dissociate soon, permitting restoration of the double bond; but a reversal of position occurs in the meantime, yielding the relatively stable trans configuration.

$$
\begin{array}{c}
\text{HC} = \text{CH} \\
| \quad\quad | \\
\text{OC} \quad\quad \text{CO} \\
\ \searrow \ \swarrow \\
\text{O}
\end{array}
\rightarrow
\begin{array}{c}
\text{HC=CH} \\
| \quad | \\
\text{HOC} \ \text{COH} \\
\| \quad \| \\
\text{O} \quad \text{O}
\end{array}
\rightarrow
\left[
\begin{array}{c}
\text{Cl} \\
| \\
\text{HC}-\text{CH} \\
| \quad\quad \| \\
\text{HOC} \quad \text{COH} \\
\| \quad\quad | \\
\text{O} \quad\quad \text{O} \\
\quad\quad\quad | \\
\quad\quad\quad \text{H}
\end{array}
\right]
\rightarrow
\begin{array}{c}
\text{O} \\
\| \\
\text{HOC} \\
| \\
\text{HC=CH} \\
\quad\quad | \\
\quad\quad \text{COH} \\
\quad\quad \| \\
\quad\quad \text{O}
\end{array}
$$
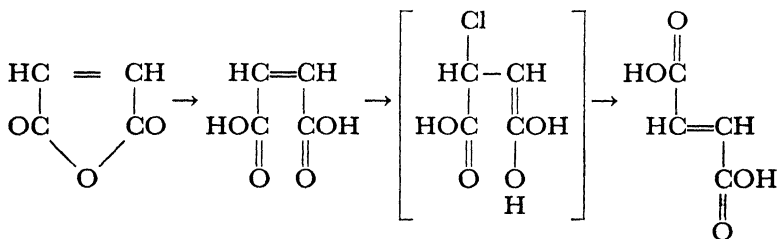
In a small flask containing 30 cc. of water heated just to the boiling point, place 25 g. of maleic anhydride. The anhydride first melts, but soon combines with water and dissolves. Cool the solution under the tap. As soon as the maximum yield of maleic acid has crystallized, collect the solid product on a Buechner filter and dry without attempt to wash. Maleic acid is very soluble in cold water; melting point when pure, 130.5°.

To the mother liquor, which contains a substantial residue of maleic acid, add 25 cc. of c.p. conc. hydrochloric acid, and reflux very gently for about 10 minutes. Crystals of fumaric acid soon separate from the hot solution, and the ultimate product is recrystallized from hot water (about 12 cc. of water required per gram

of fumaric acid), with slow cooling.   Combined yield of maleic and fumaric acids, about 25 g.   Fumaric acid sublimes above 200° C.

Slow cooling of the maleic acid solution yields larger crystals (monoclinic prisms).

Optional Experiment

392. Methyl maleate is converted with the aid of light as well as a catalyst, into methyl fumarate.   (See *J. Chem. Ed.* **18,** 477 (1941).)

EXPERIMENT 54

Decarboxylation of an Acid

393. 2,4-Dinitrophenylacetic acid, whose preparation is described in § 288, spontaneously decomposes in a simple manner at temperatures of 100° to 170°, yielding a new compound whose identity is readily proved in a subsequent experiment. Incidentally, this reaction is so nicely controllable that it may be used in a study of rate of reaction. The time required for the reaction ranges from a very few minutes at temperatures over 150° to 2 hours or more at 100°, the velocity depending not only on temperature but the acidity of the solution. It is suggested that students working in laboratories of both organic and physical chemistry combine the organic preparative experiment with an acidimetric or gasometric determination of reaction order and rate. Consult instructors.

394. Decomposition Experiment. To a 50-cc. distilling flask fit a high-range thermometer whose mercury bulb is placed at the bottom of the flask. Attach a short glass delivery tube to the side stem, and insert this tube in a test tube or beaker containing dilute barium hydroxide solution.

Introduce 2.0 g. of 2,4-dinitrophenylacetic acid into the flask, and add 15 cc. of glycerol, which is to serve as solvent. Heat the mixture to 130° to 150°; ordinarily more or less water, normally present in commercial glycerol, escapes in the form of steam. Simultaneously the decomposition reaction sets in. The temperature is slowly elevated to 170°. By this time nearly all the gaseous product of decomposition should have escaped. When the reaction is over, pour the hot mixture into a beaker containing about 200 cc. of water. Stir the mixture for a minute or two, then cool to 20° or below. Collect the semicrystalline precipitate on a Buechner filter, wash it with water, and recrystallize from about 15 cc. of methyl alcohol. If the preparation does not readily crystallize, agitate the solution, or try seeding it with a crystal of some other preparation of the same compound, such as that called for in the next section of this experiment.

NOTE. If the decarboxylation is to be conducted more slowly, as at 100° or 125°, glycerol is not the best choice of solvent. Partial esterification of glycerol, which of course is an alcohol, may take place.

395. Identification by Melting-point Method. After determining from theory what this product should be, obtain a few milligrams of a preparation of the substance made in a different manner. Determine successively the melting points of

(*a*) Your preparation.

(*b*) The second preparation used for comparison.

(*c*) A mixture of about equal quantities of the two dry crystalline substances. (See § 158.)

Problems

1. What is the importance as evidence of the three results obtained from experiments *a*, *b*, *c*, above?

2. Devise two different laboratory experiments in which the rate of decomposition of 2,4-dinitrophenylacetic acid could be measured. Specify apparatus and outline the procedures.

3. Knowing that a compound such as 2,4-dinitrophenylacetic acid should have a (theoretical) melting point somewhere in the region of 180° to 190°, predict the behavior of the substance in a conventional micro melting-point experiment. In what way do you think you might have better success in determining this supposed true melting point?

4. How might you convert "TNT" into 1,3,5-trinitrobenzene, using a reaction like that of § 394?

5. What part of the standard malonic ester synthesis reminds you of this experiment?

EXPERIMENT 55

The Diene Synthesis

DIELS-ALDER CONDENSATION

396. An unsaturated compound in which a carbonyl group is adjacent to doubly bonded carbon often condenses by 1–4 addition to a conjugated diene, causing ring closure. The present illustration, while convenient and economical in the laboratory, involves some complexity in structural representation (Bachmann and Kloetzel, 1938).
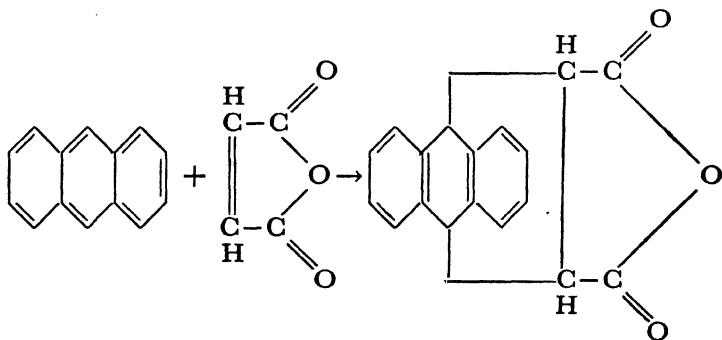
397. Anthracene-9,10-endo-α,β-succinic anhydride. In a small round-bottomed flask fitted with a reflux condenser place 2 g. of light-yellow, resublimed anthracene, as available from the experiment described in § 198, 5.6 g. of maleic anhydride, and 40 cc. of benzene. Shake the mixture with gentle heating until the solids are completely dissolved, and reflux over a water bath for 2 to 3 hours. Allow to cool slowly to room temperature, then warm slightly to dispel any turbidity due to slight crystallization of excess maleic anhydride.

Filter, and wash the pale-yellow crystalline product with 5 cc. of cold benzene. Dissolve in 75 to 85 cc. of boiling ethyl acetate,

evaporate to about 25 cc., and allow the residual solution to cool. Colorless granular crystals of the product are obtained. Yield, 2 g.; m. p., 262° to 263° (decomp.). The dried product should be bottled promptly. Exposure to moist air tends to cause hydrolysis of the anhydride portion of the molecule, a condition indicated by an opaque white coating on the crystals.

Questions

1. Represent structurally a Diels-Alder condensation of acrolein and isoprene.

2. Show how anthraquinone might be synthesized by use of the Diels-Alder reaction.

3. How may the diene synthesis be used to prove the structure of an unsaturated aliphatic compound?

4. Show how the synthesis might be used to prove the structure of 2-methyl, 3-propyl naphthalene, a compound not described in the literature.

EXPERIMENT 56

Antipyretic Drugs

398. Acetyl-*p*-phenetidine (Phenacetin). Do not interrupt this experiment at any point before recrystallization, since phenetidine has a tendency on standing to acquire a reddish, and eventually a brown discoloration. Have all reagents ready for a continuous operation. (Lumière-Barbier method, 1905.)

In a 300- or 500-cc. conical flask place 100 cc. of water, 2 cc. of conc. (12N) hydrochloric acid, and 2.6 cc. of *p*-phenetidine. Unless the phenetidine has been freshly distilled it is likely to be very dark-colored, but that is of little consequence if the preparation is still a free-running liquid. Add 2 to 3 g. of norite or equivalent decolorizing carbon, boil the mixture for 2 minutes, and filter through a fluted filter. The filtrate, dilute *p*-phenetidine hydrochloride solution, should be colorless. Cool at once to room temperature, and dissolve 2 cc. of acetic anhydride in the solution as rapidly as possible. Immediately add 0.025 mole of either anhydrous sodium acetate or the trihydrate, and shake thoroughly. Cool if necessary to 20° or below, filter, wash the crude crystalline phenacetin with cold water, and recrystallize from water. If the hot solution prepared for the recrystallization is colored, decolorize with carbon. The compound may also be recrystallized from dilute ethyl alcohol. Yield, 1.5 to 2 g. according to quality of the phenetidine. Melting point of pure acetyl-*p*-phenetidine, 137°.

399. Acetanilide may be prepared in a similar manner. Use 0.02 mole of aniline (crude dark-brown aniline oil will do) instead of the phenetidine specified above. (See also § 293.)

400. Acetylsalicylic Acid (Aspirin). The acetylation of the phenol group in salicylic acid yields a substance of great value as a fever-depressant, which is much less toxic than acetanilide, formerly much used for the purpose.

$$\text{OH} \atop \text{COOH} \;+\; (CH_3CO)_2O \;\rightarrow\; {\text{OCOCH}_3 \atop \text{COOH}} \;+\; CH_3COOH$$

281
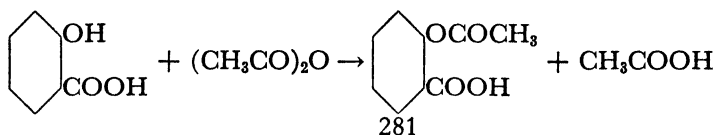
In a small flask heat a mixture of 3 g. of salicylic acid, 6 g. of acetic anhydride, and 3 drops of conc. sulfuric acid to 50° for 10 or 15 minutes, using a water bath. Now cool the reaction mixture in an ice bath, with stirring, until it thickens to a crystalline, semisolid mass. Add 50 cc. of water, stir until a thin sludge remains, and filter. The solid product is crude acetylsalicylic acid, or aspirin. Dry the product in the open air, and dissolve in the minimum volume of gently boiling ether, heated under reflux condenser over the steam bath. To the resulting solution add an equal volume of light ligroin (petroleum solvent) or petroleum ether, and allow to stand on ice for several hours. Collect the resulting purified crystals on the Buechner filter and dry in the open air. The melting point of pure acetylsalicylic acid is not definite, on account of slight decomposition. Figures around 128° to 133° are likely to be obtained. Yield, 3 g.

401. Ferric Chloride Test. Add a few drops of aqueous ferric chloride to a solution made by dissolving a few crystals of each of the following in 5 cc. of water in a test tube.

(*a*) Salicylic acid.

(*b*) Pure aspirin.

(*c*) Your preparation of aspirin.

The appearance of a striking coloration indicates free phenolic hydroxyl groups.

EXPERIMENT 57

Sulfanilamide

$CH_3CONHC_6H_5 \rightarrow CH_3CONHC_6H_4SO_2Cl \rightarrow$
$ CH_3CONHC_6H_4SO_2NH_2 \rightarrow H_2NC_6H_4SO_2NH_2$
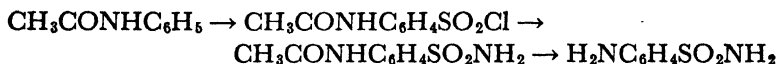
402. Chlorosulfonation. Provide an ice bath, and either work in a hood or use a delivery tube and vapor trap as shown in § 251. In a 200- or 250-cc. conical flask place 25 cc. of chlorosulfonic acid, which should be handled carefully, since it may cause skin burns. Add gradually 10 g. of crystalline acetanilide, using the ice bath to keep the reaction temperature between 10° and 20°. Heat the final reaction mixture on the steam bath for about 30 minutes, cool to room temperature, and pour with stirring into 150 to 200 cc. of a thin slush of ice and water. Collect the granular product of p-acetaminobenzenesulfonyl chloride on a Buechner filter, wash with cold water, and use at once in the next procedure.

403. Treatment with Ammonia. To the acid chloride just prepared, which has been returned to the reaction flask, add 35 cc. of conc. aqueous ammonia (sp. g. 0.90) and 35 cc. of water (or use 70 cc. of about 8N NH₄OH). Mix thoroughly, and heat gently to near the boiling point for 20 to 30 minutes. Cool the solution and add hydrochloric acid until the mixture is neutral to litmus. Filter, wash the product of p-acetaminobenzenesulfonamide with water, and carry to the next step.

404. Hydrolysis to Sulfanilamide. To the amide product just prepared add 25 cc. of 3N hydrochloric acid, and boil cautiously—avoiding charring—for 15 or 20 minutes. If necessary, decolorize the solution with carbon, and add to the filtrate 10 g. of sodium bicarbonate. Collect the product of sulfanilamide on a filter, wash with cold water, and dry; or recrystallize from hot water, using a stemless funnel in the process. Yield, 7 g. Melting point of pure

sulfanilamide, 163°. Students are warned that this substance should not be used in treatment of illness except on advice of a physician.

Questions

1. What is the objection to the presumably simple, direct procedure from an inexpensive raw material: sulfanilic acid → sulfanilyl chloride → sulfanilamide?

2. Why do we use sodium bicarbonate to neutralize the solution in the last procedure rather than sodium hydroxide?

EXPERIMENT 58

Amino Acid

405. When an aliphatic α-chloro or α-bromo- acid is treated with ammonia, the halogen atom is replaced by the primary amine group —NH₂. An amino acid is produced along with the by-product of ammonium halide. In the example given below it has been found that the presence of considerable ammonium carbonate leads to better yields (Cheronis, 1941).

$$ClCH_2COOH + 2NH_3 \rightarrow NH_2CH_2COOH + NH_4Cl$$
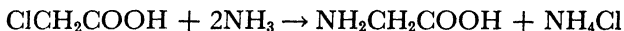
406. Glycine (Aminoacetic Acid.) In a 500- or 700-cc. flask dissolve 90 g. of powdered ammonium carbonate (commercial product containing some carbamate) in 120 cc. of warm water (50° to 60°) and add 100 cc. of conc. ammonium hydroxide (sp. g. 0.90). To this solution add slowly, with swirling of the flask, a solution of 0.25 mole of chloroacetic acid (95 to 100%) in 35 cc. of water. (Keep chloroacetic acid away from the skin.) Stopper the flask tightly and allow to stand, preferably in a warm place, for at least 24 hours.

At the next laboratory period distil the reaction mixture either in the manner suggested in the accompanying figure or in whatever other way avoids the nuisance of ammonia fumes in the laboratory, until the volume has been reduced to 75 cc. During this process, particularly toward the end, avoid heating at the margin of the liquid which would cause charring. If the solution is not colorless, treat with about 1 g. of decolorizing carbon. (See § 109.) Add to the clarified filtrate 250 cc. of methanol (95 to 100%), mix thoroughly, and set aside in a refrigerator for 6 hours or more for crystallization of glycine.

The resulting product of crude glycine contains ammonium chloride as a major impurity. This by-product may be largely removed by suspending the crystals in 50 cc. of methanol for 5 to 10 minutes, and filtering. More thorough purification is accomplished by dissolving in water and reprecipitation with methanol. Yield, 13 g.

The compound does not have a sharp melting point, but chars at about 235°.

The presence of any appreciable quantity of ammonium chloride, not acceptable to biochemists who have considerable use for glycine, is detected by tasting, which is quite safe, since neither the chloride
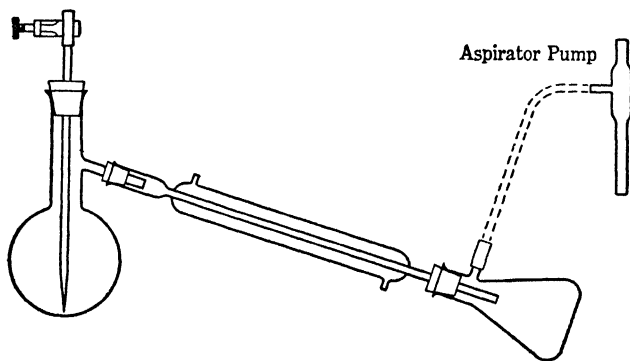
nor glycine are toxic. Ammonium chloride has a sharp, salty taste, while pure glycine is sweet. Special quantitative determination of ammonia or chloride may also be carried out.

REACTIONS OF AN AMINO ACID

407. Amphoterism—Two Methods of Salt Formation. (*a*) Dissolve 1 g. of glycine in 25 cc. of hot water, and drop in particles of cupric carbonate until the resulting reaction ceases. Heat to boiling, decant the clear blue liquid, and cool. Beautiful blue crystals of the sparingly soluble cupric salt separate, illustrating a reaction with the carboxyl group.

(*b*) Dissolve 1 g. of glycine in the smallest possible quantity (a few drops only) of boiling C.P. conc. hydrochloric acid. Upon cooling, crystals of the amino-acid hydrochloride separate, illustrating a reaction with the amine.

408. Effect of Formaldehyde. Dissolve 0.5 g. of glycine in 5 cc. of water in a test tube. Add a drop of methyl red indicator solution. If the glycine is pure, a yellow color will be obtained, since glycine is nearly neutral in reaction. If a reddish or orange

tint is observed, acidic impurities are present, causing a change in pH value to some point below 6. In such a case touch the solution cautiously with a stirring rod which is wet with very dilute ammonia or sodium hydroxide, thus obtaining a yellow color. Now treat a 3- to 5-cc. sample of conc. formaldehyde solution (15 to 35%) with methyl red, and neutralize it in the same way if necessary. Mix the two yellow solutions. The formaldehyde reacts with the amine group. Explain the change in color.

409. Reaction with Nitrous Acid. To a solution of about 0.5 g. of sodium nitrite in 5 cc. of cold water add a few drops of acetic acid. A few minute bubbles appear, indicating slight decomposition of the nitrous acid formed. Now drop in a few crystals of glycine. What is the gas formed? In what way could this experiment be made quantitative? What difficulties might arise?

Optional Syntheses

410. Glycine may be prepared by the aldehyde ammonium cyanide method (Ref. 4).

dl -**Alanine** (*a*-Aminopropionic Acid) may be prepared from *a*-bromopropionic acid (§ 368) by a reaction similar to that of § 405. (See *J. Org. Chem.* **6,** 374 (1941).

Cystine from Hair. This experiment illustrates the hydrolysis of protein to give an optically active natural amino acid, in this case one containing sulfur (Refs. 5, 27, 30, 32).

Tyrosine. (Refs. 27, 32, 35.)

Glutamic Acid. (Refs. 5, 27.)

411. The Schotten-Baumann Reaction. When a primary amine is mixed with an acid chloride in the presence of aqueous alkali, the reaction to produce an amide is more rapid than that of ordinary hydrolysis.

$$RCOCl + NH_2 . CH_2COOH + NaOH \rightarrow$$
$$RCO . NH . CH_2COOH + NaCl + H_2O$$
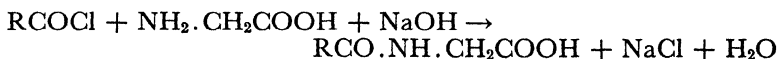
412. Hippuric Acid (Benzoyl-aminoacetic Acid). Dissolve 3 g. of glycine in its equivalent of 1N sodium hydroxide solution in a 200- or 300-cc. flask. Place a piece of litmus paper in the flask and add in small portions a quantity of benzoyl chloride about 15% in excess of that required by theory to react with the glycine. After adding each portion, stopper the flask and shake well until all of the

chloride has reacted. The mixture must be kept slightly alkaline, with the aid of additional sodium hydroxide if necessary. (NOTE. Benzoyl chloride is very offensive; work in a hood or outdoors.) Cool the reaction mixture under the tap if it gets warm. Finally eliminate paper or other solid material by filtration, and then place in the solution a piece of Congo Red indicator paper.

On a second piece of Congo Red paper place one drop of 6N hydrochloric acid, and then allow a few drops of water to run upon the acid spot and spread downward on the paper. Notice the appearance of a deep-purple shade, to be used for comparison.

Using an eyedropper, and stirring the reaction mixture effectively, add just enough dilute (6N) hydrochloric acid to turn the Congo Red paper from deep red to purple, as above described. Cool the flask and allow the mixture to stand for 10 minutes or more.

Collect the resulting crystalline precipitate of hippuric acid (benzoyl-glycine) upon the Buechner filter and dry in a vacuum desiccator. When the crystals are thoroughly dry, place in about 25 cc. of carbon tetrachloride and boil very gently in a beaker under a watch glass for about 5 minutes. Filter the mixture while hot, and repeat the treatment, which is virtually an extraction of benzoic acid from the preparation. Finally wash the crystals with diethyl ether and dry again in the desiccator. Yield, 85% of the theoretical. Melting point of hippuric acid, 187°.

413. Synthesis in the Human Body. If benzoic acid or a suitable one of its salts is introduced into the human digestive system, the benzoyl radical of the substance soon combines with an equivalent quantity of glycine, yielding the amide, hippuric acid, which is then eliminated in the urine, from which it may be recovered by crystallization. Sodium benzoate of chemically pure or U.S.P. grade, commonly used as a food preservative, is selected as more palatable than the free acid.

Just before retiring at night drink a solution of 5 g. of pure sodium benzoate in a half glassful of water. Next morning preserve the urine and proceed with the laboratory experiment on that same day. For each 100 cc. of urine add 25 g. of clean solid ammonium sulfate and 1.5 cc. of conc. sulfuric acid, stirring until the salt is completely dissolved. Cool the mixture in a refrigerator for several hours, or until a maximum crystallization of hippuric acid has been attained.

Filter, and recrystallize the solid product from about 50 cc. of hot water with the aid of decolorizing carbon (see § 109), and boil the mixture 10 minutes or more. Cool the final filtered solution for an hour in an ice bath, and collect the purified hippuric acid upon a filter.

EXPERIMENT 59

The Skraup Synthesis

414. Quinoline. Acrolein condenses with aniline at both ends of the aliphatic chain, causing ring closure and the formation of a heterocyclic compound. A small amount of oxidation is necessary to complete the process. Glycerol is an inexpensive source of the acrolein reagent which presumably is the active material in the ring closure.
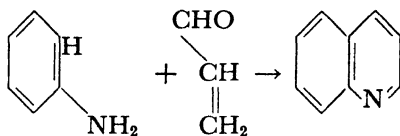
In a 2-l. round-bottomed flask, equipped with a water-cooled reflux condenser, place successively, in the order named, 10 g. of ferrous sulfate (heptahydrate), 108 g. of anhydrous glycerol, 27 g. of redistilled aniline, and 21 g. of redistilled nitrobenzene. (Anhydrous glycerol may be prepared by heating commercial glycerol to 180° in an open evaporating dish.) Mix the reagents thoroughly and add slowly, with shaking, 50 cc. of conc. sulfuric acid. The resulting aniline sulfate should nearly all remain in solution.

With the reflux condenser in place, cautiously heat the flask over wire gauze until the mixture boils. (Careless heating may cause a violent ebullition.) For some time the heat of reaction is sufficient to maintain the boiling temperature and later a burner is employed. Boil the mixture for 3 to 4 hours; then cool the mixture below 100°, add 50 cc. of water, and pass a current of steam through the material until the excess nitrobenzene has been expelled.

To the residue in the steam flask add a cool solution of 85 g. of sodium hydroxide in 250 cc. of water. Again pass steam through the material, this time collecting the distillate of water, quinoline, and aniline in a second 2-l. flask used as a receiver. This distillation is continued as long as oily products come over. Add 20 cc. of conc.

sulfuric acid to the mixed distillate. Cool this solution to 0° and add a concentrated solution of sodium nitrite until a drop of the reaction mixture colors potassium iodide-starch mixture a deep blue or purple instantly. As this diazotization process approaches completion, the reaction becomes slow. It is not considered to be complete until the aniline mixture, after a 5-minute interval with stirring, gives—instantly—a positive test for excess nitrous acid. From 6 to 8 g. of sodium nitrite will be required.

With the aid of a water bath heat the diazotized solution for an hour, and then add a solution of 40 g. of sodium hydroxide in 150 cc. of water, cooling the flask under the tap. Steam-distil the mixture, and saturate the distillate with common salt. Extract with ether, dry the extract over potassium hydroxide, filter, and remove the ether by distillation. (See § 90 for discussion of special technique in such distillation.) Distil the ether-free quinoline through an air-cooled condenser. Yield, 30 g. Boiling range, about 235° to 238°. Although colorless when pure, quinoline from this process has a pale-yellow tint. Reduced-pressure distillation of the final product is desirable but not necessary.

Questions

1. How might one determine whether the aldehyde end of such a molecule as acrolein combined with the ortho position, as shown structurally above, or in reverse position with the amine group?

2. Why was so unusual an oxidizing agent as nitrobenzene employed?

3. Why was the mixture diazotized?

4. What is the purpose of the 40 g. of sodium hydroxide used after diazotization?

SUPPLEMENTARY EXPERIMENTS

415. Synthetic Sequences. Valuable experience in synthesis is derived from the completion of a sequence of preparations in which one product becomes the starting material for the next. In a literature search for directions it is advisable first to seek information on the final product desired. The sequence is then traced backward. Consult the instructor or assistant before attempting any of these sequences, with particular attention to quantities of starting materials.

After approval by the instructor, a report is written in the notebook, with full information as to literature sources, before laboratory work is started. It is desirable first to see whether any part of the procedure has been handled in *Organic Syntheses* or other modern laboratory manuals (see reference list, § 175). Next come the original research papers. Information from such sources is traced to advantage by first consulting the following reference books in the order given.

Beilstein's *Handbuch der organischen Chemie*, 4th ed., and Richter's *Lexikon*.

Beilstein, supplementary volumes, and Stelzner (sequel to Richter).

Chemical Abstracts and *Chemisches Zentralblatt*, starting with the volumes for 1929 if the above handbooks have already been covered; then trace down to date.

1. *n*-Butyl alcohol, butyl bromide, butyl cyanide, valeric acid, butyl valerate.
2. *n*-Butyl alcohol, butyl bromide, butyl magnesium bromide, *n*-hexyl alcohol. (Use of ethylene oxide.)
3. *iso*-Propyl alcohol, acetone, pinacol, pinacolone, dimethylbutadiene.

4. Chloroacetic acid, diethyl malonate, diethyl *n*-butyl malonate, *n*-caproic acid, α-bromo-*n*-caproic acid, norleucine.

5. *sec*-Butyl alcohol, methyl ethyl ketone, nitroso methyl ethyl ketone, dimethylglyoxime (reagent for nickel).

6. Cyclohexanol, adipic acid, cyclopentanone.

7. Nitrobenzene, *m*-dinitrobenzene, *m*-nitroaniline, *m*-nitroiodobenzene.

8. Nitrobenzene, hydrazobenzene, benzidine, Congo Red.

9. *o*-Nitrotoluene, *o*-nitrobenzoic acid, *o*-aminobenzoic acid, diphenic acid, or Methyl Red indicator.

10. *p*-Nitrotoluene, *p*-nitrobenzoic acid, *p*-aminobenzoic acid, *n*-butyl *p*-aminobenzoate (butesin, local anaesthetic).

11. *p*-Nitrotoluene, 2,4-dinitrotoluene, TNT, 2,4,6-trinitrobenzoic acid, 1,3,5-trinitrobenzene, 3,5-dinitroanisole.

12. Benzyl chloride, benzyl cyanide, *p*-nitrobenzyl cyanide, *p*-nitrophenylacetic acid, *p*-aminophenylacetic acid, *p*-bromophenylacetic acid.

13. Aniline, acetanilide, *p*-nitroacetanilide, *p*-nitroaniline, Para Red (pigment).

14. Aniline, acetanilide, *p*-bromoacetanilide, *p*-bromoaniline, *p*-bromochlorobenzene.

15. *p*-Toluidine, aceto-*p*-toluidide, 3-nitro-4-acetoaminotoluene, 3-nitro-4-aminotoluene, *m*-nitrotoluene.

16. *p*-Toluidine, aceto-*p*-toluidide, 3-bromo-4-acetaminotoluene, 3-bromo-4-aminotoluene, *m*-bromotoluene.

17. Chlorobenzene, 2,4-dinitrochlorobenzene, 2,4-dinitrophenol, 2,4-diaminophenol hydrochloride (photographic developer "Amidol").

18. Aniline, thiocarbanilide, phenyl mustard oil, triphenylguanidine.

19. Phenol, sodium *p*-hydroxyphenyl arsonate, 3-nitro-4-hydroxyphenylarsonic acid, arsphenamine (salvarsan).

20. Phenol, phenetole, *p*-nitrophenetole, *p*-phenetidine, acetyl-*p*-phenetidine ("Phenacetin," drug).

21. Phenol, *o*-nitrophenol, *o*-nitroanisole, *o*-anisidine.

22. Bromobenzene, 2,4-dinitrobromobenzene, 2,4-dinitrophenylhydrazine.

23. Bromobenzene, 2,4-dinitrobromobenzene, 2,4-dinitrophenol, picric acid.

24. α-Naphthol, 1-naphthol-2,4-disulfonic acid, 2,4-dinitro-1-naphthol, 2,4-diamino-1-naphthol, amino-α-naphthoquinone (Ref. 31).

25. p-Toluenesulfonic acid, p-toluenesulfonyl chloride, sodium p-toluenesulfinate, p-tolylmercuric chloride, p-chloromercuribenzoic acid, p-iodobenzoic acid.

26. Pinene, pinene hydrochloride, camphene, isobornyl acetate, isoborneol, camphor (Ref. 33).

416. Preparations from the Original Literature. For this experiment there is chosen an organic compound whose preparation is not described in any laboratory manual. Original research reports are consulted, including the "discovery" paper, in which the compound under consideration was reported for the first time. Furthermore, not even the original paper may give full directions. Analogous preparations are then traced. Beilstein's *Handbuch* is invaluable in such work.

It is characteristic of the average student, after a few weeks of laboratory experience with hand-picked experiments as found in manuals, that he will tackle synthetic projects far beyond available time and present skill. Reactions selected uncritically from an ordinary textbook of organic chemistry should invariably be submitted to the instructor for approval. Much grief is thus avoided.

417. New Organic Compound. The preparation of a compound not described in the literature often presents interesting possibilities. A complete novelty of this type is most easily obtained by combining two relatively uncommon organic compounds in some form of anhydride linkage. For example, an uncommon organic acid may be converted into a substituted amide, or an ester. More useful, but probably more difficult, assignments of this sort may be arranged by a search of tables of compounds in manuals of qualitative organic analysis, as cited in § 423. Many members of various homologous series are still missing, and a determination of their properties would be a valuable service to research workers. If the new compound is of sufficient importance, and the work carefully done, a brief report may well go to the *Journal of the American Chemical Society*, which maintains a special department in each monthly issue for this purpose. To be acceptable in such a journal, the report must show that the compound was adequately purified, the melting

or boiling point accurately determined, and a satisfactory quantitative elementary analysis performed to prove the identity of the product.

418. Special Syntheses. Certain organic preparations are of special interest, either for their practical applications or for unusual features of technique, as follows.

3-Aminophthalhydrazide ("Luminol") emits light when gently oxidized, illustrating beautifully the phenomenon of chemiluminescence. See *J. Chem. Education*, **11,** 142 (1934).

Phenylnitromethane is a compound which exists in two tautomeric forms, which can actually be prepared in the laboratory. See Ref. 34.

Tetraphenyl ethylene glycol, usually loosely named "benzopinacol" or "tetraphenylpinacol," illustrates a photochemical synthesis. See Ref. 41.

Triphenylmethyl is the classical illustration of a compound of trivalent carbon. See Refs. 18, 20, 28, 31.

Naphthidine, similar in fundamental structure to benzidine, is used as an oxidation-reduction indicator. See *Ind. Eng. Chem. Anal. Edition*, **8,** 306 (1936).

Copper Phthalocyanine (Monastral Blue). A unique heat-resistant organic pigment. See Ref. 33.

Furfural, a heterocyclic aldehyde, is prepared from corn cobs. See Refs. 1, 6.

Ketene ($CH_2 = CO$), a powerful acetylating agent, is prepared by pyrolysis of acetone, employing either gas or electric heating. See *Organic Syntheses, Collective Volume I*, 2d ed., and *J. Org. Chem.* **5,** 122 (1940).

Nicotinic acid is prepared from nicotine. See Ref. 4.

Caffeine is prepared from commercial tea leaves. See Refs. 27, 29, 30, 35, 39.

β-Naphthyl methyl ether (Nerolin) is an important perfume ingredient. See Refs. 28, 29, 30, 35, 38, 45.

Atophan (Cincophen) an analgesic drug, is a heterocyclic compound prepared by ring closure. See Ref. 42.

QUALITATIVE ORGANIC ANALYSIS

TESTS FOR ELEMENTS

419. Carbon. If a substance is not so volatile that it escapes from the apparatus before reaction, it may be identified as a compound of carbon by combustion. The material is mixed with powdered cupric oxide and strongly heated in a hard-glass test tube with delivery tube leading into limewater. A white precipitate of calcium carbonate reveals the presence of carbon dioxide.

420. Halogens. In the Beilstein test for halogens, a loop of copper wire is first freed of any possible halide salts by holding in a blue flame. The absence of green color in the flame shows that the wire is ready for the test. The loop is cooled, dipped into the liquid or powdered solid under investigation, and returned to the flame. A flash of green color in the flame indicates that the unknown substance contains chlorine, bromine, or iodine. If the substance is volatile, it may be difficult to obtain more than a fleeting trace of the green color, which indicates only a momentary reaction of copper with halogen. If it is necessary to distinguish the particular halogen, try the procedure of § 421, in which the appropriate silver halide is formed.

In the Beilstein test care must be taken neither to jump to conclusions based on inorganic impurities, nor to decide that halogen is absent when volatility may be cause of the negative result.

421. Nitrogen, Sulfur, and Halogens. Using a small blast flame, prepare a miniature test tube by closing one end of a piece of 8- or 10-mm. glass tubing about 8 cm. long. (The commercial 3-by-3/8-inch test tube is a fairly good ready-made substitute, but not equal to the tube above suggested on account of its thin-walled construction.)

Place a clean piece of metallic sodium about the size of a small pea in the tube described above. Heat the tube—cautiously at first to

337

avoid cracking the newly closed end—until the sodium has not only melted, but has evolved metallic vapor which lies in a dull mass over the metallic surface. Hold the tube out at a safe distance, with its open end pointed away from the face, and drop in about 0.25 g. of the finely divided substance under investigation. If the substance is suspected of being a sulfonic acid, use a smaller quantity, lest there be insufficient sodium to reduce the sulfur completely. Continue to apply the flame until all parts of the tube at one time or another have reached a bright-red heat. It is very important that no partially decomposed organic matter be left, lest the subsequent tests be obscured by brownish colloidal matter.

While the tube is still hot, hold it out at arm's length and cautiously lower it into a small beaker containing 10 cc. of distilled water; but do not allow the hot closed end to do more than barely touch the surface of the water. Usually the tube cracks, admitting air and permitting residual melted sodium to burn quietly, with its customary intensely yellow flame. Keep the face away from the beaker—and preferably keep the side wall of the beaker between the sodium and the eyes.

After the possible sodium residue has been burned as completely as the cracked tube permits, drop the tube while it is still hot into the water in the beaker. The lower part of the tube is now likely to be shattered. In view of the possibility of metallic sodium still being present when this last operation is conducted, beware of flying globules of the metal.

There should now be nothing remaining in the beaker but broken glass, particles of pure-black carbon, and a solution possibly containing the following substances, now in the form of ordinary sodium salts:

Cyanide—if the original substance contained nitrogen.
Sulfide—if the substance contained sulfur.
Chloride, bromide, iodide—if the substance contained halogen.
Hydroxide—from the excess sodium not used otherwise.

Other compounds may be present if metallic constituents were present in the original preparation. These are not considered here, and may usually be ignored in the subsequent procedures.

Filter the alkaline solution and divide the filtrate into three equal portions. To one add 2 cc. of ferrous sulfate solution and one drop

of ferric chloride solution, and boil for 1 minute. This procedure allows the cyanide to unite with ferrous iron to give ferrocyanide. Acidify the mixture with dilute hydrochloric acid; this frees ferric ion, which was temporarily out of solution owing to the precipitating action of the alkaline solution on the ferric chloride reagent. Any possible ferrocyanide present will now immediately react with ferric ion to produce the intensely blue ferric ferrocyanide. Unfortunately this blue compound is often peptized, or held for a time in a colloidal suspension of uncertain greenish-yellow tint.

Pass the reaction mixture through a common filter. The filter paper fibers will hold back, or adsorb, the blue precipitate. If the filter is now washed, the characteristic bright-blue color will be revealed, indicating nitrogen in the original substance.

$$\text{Nitrogen Compound} \rightarrow CN^- \rightarrow Fe(CN)_6^{\bullet} \rightarrow Fe_4Fe[(CN)_6]_3$$
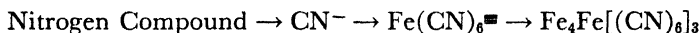
To a second portion add 5 cc. of dilute acetic acid and a few drops of lead acetate solution. A characteristic brownish-black precipitate of lead sulfide indicates the presence of sulfur.

Acidify the third portion with dilute nitric acid. If the original compound contained nitrogen, boil this third portion for 1 minute to destroy cyanide, cool, and add a few drops of silver nitrate solution. A flocculent precipitate indicates the presence of halide.

Silver chloride—white.

Silver bromide—pale yellowish-white.

Silver iodide—yellow.

If there is still doubt as to which halogen is present, or if more than one halogen might be present, consult a manual of inorganic qualitative analysis.

IDENTIFICATION OF AN ORGANIC COMPOUND

422. This experiment is designed as an illustration of organic qualitative analysis, a phase of chemistry which is often taken up in a substantial laboratory course given in the senior or graduate year. Experience has shown such a course to be one of the most interesting and instructive in the chemical curriculum.

Obtain a sample of an "unknown" organic compound, which is not necessarily pure but is not intentionally mixed with any other material unless notice to the contrary is given. Before a report on

the identity of the compound is accepted by the instructor the student is required to prepare a small amount of a purified derivative, whose melting point or other characteristic property indicates that his conclusion is correct.   There is no necessity of preparing even as much as 1 g. of the derivative, if not convenient or economical of materials.   Quality alone is of significance.

The substances issued in this experiment are arbitrarily restricted, for the sake of economy of reagents and simplicity, to the following:

Aliphatic alcohols, acids, esters, amines and salts.

Aromatic hydrocarbons, halides, phenols, acids, esters, salts, amines, amides, and nitro-compounds, in each case containing not more than one aromatic ring in the molecule.

No compounds are considered in which more than one kind of salt- or ester-forming group is present in the molecule.   Thus a nitrotoluidine or a dichlorophenol might be issued, but not sodium salicylate or an aminobenzoic acid.

423. A favorite scheme for narrowing down the search is that of classification by solubility, which is first employed.   More elaborate versions of such a solubility table are to be found in the excellent works of Kamm (*Qualitative Organic Analysis*) and Shriner and Fuson (*The Systematic Identification of Organic Compounds.*)

424. Method of Testing Solubility.   Test very small portions of the unknown substance in various solvents or liquid reagents as suggested in the outline below.   If the "unknown" is solid, and is not soluble in 20 to 25 parts of the solvent, it is regarded in the following outline as "insoluble."   If the material is liquid, it must dissolve completely in 10 to 15 parts of solvent to be classed as "soluble." Note that some substances, while soluble in certain solvents, do not dissolve rapidly, and thus may mislead the observer.   A negative decision should not be recorded until a test has been made with the solvent when heated.   If the heated solvent dissolves the substance, cool the resulting solution.   If the substance is to be classed as "insoluble," it should then separate from the solution, unless it has reacted chemically with the solvent.   Perhaps a "seed crystal" may be needed.

425. Outline of Procedure.   Assuming that compound types are limited to those listed for this experiment, follow these tests strictly in the order given.

A. **Soluble in cold water.**
    1. *Soluble in ether*: aliphatic alcohols, acids, esters and amines of low molecular weight; some phenols.
    2. *Insoluble in ether*:
        a. Acid reaction to litmus: amine salts.
        b. Neutral or slightly alkaline: ammonium salts, salts of metals.

B. **Insoluble in cold water.**
    1. *Soluble in dilute (about 0.5 N) HCl*: amines.
    2. *Soluble in dilute (about 1N) NaOH*:
        a. Soluble in $NaHCO_3$: carboxylic acids, nitrophenols.
        b. Insoluble in $NaHCO_3$: phenols.
    3. *Insoluble in HCl or NaOH*.
        a. Contains nitrogen (see § 421).
            (1) Hydrolyzable: amides ($RCONH_2$, $RCONHR'$.)
            (2) Unhydrolyzable: nitro compounds.
        b. Contains no nitrogen.
            (1) Soluble in cold, conc. H_2SO_4.
                (*a*) Hydrolyzable: esters.
                (*b*) Unhydrolyzable: aliphatic alcohols of higher molecular weight.
            (2) Insoluble in cold, conc. H_2SO_4.
                (*a*) Contains halogen: aromatic halide.
                (*b*) Contains no halogen: aromatic hydrocarbon.

426. Tests for Elements. If the question has not already been settled in the solubility experiment, the presence or absence of nitrogen, chlorine, bromine, and iodine should now be established. See § 421 for directions. *Beware of mistaking an impurity* for the main component. For example, many a student has wasted hours of laboratory time because he encountered a trace—or perhaps 1%— of common salt in his "unknown" and jumped to the conclusion that he was dealing with an alkyl or aryl chloride. As already suggested, purification should precede the tests.

427. Special Tests. Since the solubility experiment does not locate every type of compound distinct from all others, special tests are needed for certain final differentiations. A few important examples of these are given in §§ 428 to 440; others are to be found in the special textbooks cited.

428. Physical Properties. With the compound now classified— for example, as an aliphatic alcohol, or primary aromatic amine—

the balance of the problem of identification involves use of a combination of confirmatory class tests, such as appear in following paragraphs, with a search of handbook literature. Color, boiling point, melting point, density, etc., may be of importance. Final identification is confirmed by preparation and physical test of the required derivative.

429. Alcohols. These react with metallic sodium to yield hydrogen. Be sure that water, or other impurity of even faintly acidic character, is absent before drawing conclusions. Practically all liquids in ordinary storage have at least traces of water, and will give evidence of hydrogen at first. If the evolution of hydrogen persists, with continued production of a salt in quantity, then the presence of an alcohol is suggested. Watch out for enols, slightly acidic amides, etc., and do not take the sodium test too seriously without close investigation.

Primary, secondary, and tertiary alcohols are distinguished by the variance in their ability to form chlorides when treated with concentrated hydrochloric acid (Lucas's test; see Kamm, p. 149).

430. Acids. The simpler aliphatic acids may be distinguished by the Duclaux method. (See §§ 71, 262.) Less volatile acids are identified through a determination of equivalent weight. Aromatic acids are solids. The determination of equivalent weight is often useful.

431. Esters. Devise a short experiment, using ideas from the experiments on "Equivalent Weight of an Ester" (§ 259) and "Hydrolysis of an Ester" (§ 262).

432. Amines. Aliphatic amines are decidedly basic. A salt is formed in conspicuous fashion when a few drops of such an amine are treated with a few drops of conc. hydrochloric acid. Aromatic amines are much weaker, but the primary amines are still strong enough for definite salt formation. (Secondary and tertiary amines with two or more benzene rings are too weak for satisfactory salt formation, but are excluded by structure from this experiment.)

433. Nitrous Acid Tests for Amines. Nitrous acid is often used to distinguish the three types of amines. To a few drops, or 0.5 g., of the unknown amine, dissolved in 5 cc. of cold (0° to 5° C.) 2N hydrochloric acid, add a few drops of aqueous sodium nitrite:

(a) Primary aliphatic amines at once yield nitrogen gas. (NOTE. Do not mistake nitric oxide or dioxide for colorless, insoluble *nitrogen* gas.)

(b) Primary aromatic amines do not produce nitrogen at these low temperatures, but are instead diazotized. Add a few drops of the reaction mixture to a solution of 0.1 g. of β-naphthol in 5 cc. of 2N sodium hydroxide. An azo dye is formed.

(c) Secondary amines yield insoluble yellow oils, denser than water.

(d) Tertiary aliphatic amines give no significant tests (form unstable salts).

(e) Tertiary aliphatic-aromatic amines (for instance, dimethylaniline); where the structure of the molecule permits, these form green paranitroso compounds whose hydrochlorides are yellow. (See § 320.)

434. Benzenesulfonamides: Hinsberg Test. A primary or secondary amine, containing replaceable hydrogen atoms bound to nitrogen, reacts with benzenesulfonyl chloride, yielding in each case a substituted sulfonamide of properties usually quite different from those of the original amines. A tertiary amine under such conditions is unreactive and thus at once distinguished. Of the two types of sulfonamides, only that from the primary amine displays acid properties whereby it may dissolve in dilute sodium hydroxide.

$$C_6H_5SO_2.NHR + NaOH \rightarrow C_6H_5SO_2NNaR$$
$$C_6H_5SO_2.NR_2 + NaOH \rightarrow \text{(no reaction)}$$
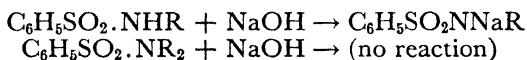
Aniline, methylaniline, and dimethylaniline are successively tested as follows.

To 5 cc. of 3N sodium hydroxide in a test tube add 6 drops of the amine and 8 drops of benzenesulfonyl chloride. Shake vigorously until the odor of the chloride has disappeared. In the case of dimethylaniline the amine remains unreacted in the form of oil droplets. With methylaniline or aniline a new product is formed, which may temporarily appear in oily form, but soon solidifies, especially if the inner wall of the tube is scratched with a stirring rod in contact with the product. Insolubility of this material in dilute sodium hydroxide indicates that a secondary amine has been used. If no solid is produced, acidify the alkaline reaction mixture with

dilute hydrochloric acid, thus precipitating the sulfonamide of the primary amine, which in turn is alkali-soluble.

435. Phenols. Although a phenol seems to fall into the class of an alcohol, judging by mere structure, it is not typical of that group. A phenol is normally strong enough as an acid to dissolve in sodium hydroxide, but not in bicarbonate. Phenols also give striking colors when treated with ferric chloride.

436. Salts. Most common salts are either of an inorganic base and organic acid, or vice versa. The former is usually a metallic salt, and usually is recognized by its extremely high melting point, or even infusibility. When the solid is heated to ignition on a piece of platinum foil or crucible cover, a noncombustible residue or ash is left, whereas most purely organic compounds disappear. Treatment of the solid salt with conc. sulfuric acid will free the organic component, which can be distilled if volatile and stable. Treatment of a solution of the salt with hydrochloric acid normally precipitates the acid if it be aromatic. If it is a salt of a dibasic acid of low molecular weight, more trouble is experienced because of the high solubility and low volatility of the acid. Consult reference books describing these acids.

Ammonium salts of organic acids leave no ash on ignition, but otherwise are treated like metallic salts. The ammonium component is recognized by the great readiness with which ammonia is expelled when the salt is merely mixed in the cold with sodium hydroxide. Amine salts so treated may yield a volatile organic amine; or the amine may simply separate as an oil, as in the case of high-boiling aromatic amines.

437. Amides. Amides of the simple $RCONH_2$ type yield their ammonia content only after gentle heating with caustic alkali. Substituted amides, such as anilides, after prolonged heating, yield the corresponding amines, usually as discolored oils which float upon the surface of the concentrated alkali solution.

438. Aromatic Nitro Compounds. These substances are usually insoluble in water, dilute acid and dilute alkali, unless they contain acidic or basic groups which react with either of the latter two reagents. They are reduced in the presence of tin and hydrochloric acid, being changed to primary amines which immediately form hydrochlorides and thus dissolve in water.

Many, but by no means all, of the simpler nitro compounds may be reduced with zinc in neutral solution, yielding aryl hydroxylamines which in turn reduce ammoniacal silver. Before trying the following test, be sure that there is not already some group in the compound which reduces ammoniacal silver. No conclusions should be drawn from negative results:

Dissolve a few drops, or about 0.2 g., of the supposed nitro compound in 5 cc. of hot alcohol. To this solution add a few drops of a concentrated solution of calcium chloride, and a pinch of zinc dust. Heat to boiling, allow to stand for 3 minutes, and filter. To the filtrate add 2 cc. of dilute (6N) ammonium hydroxide and a few drops of silver nitrate solution. A muddy gray precipitate of metallic silver indicates that the original compound was a nitro compound, provided it did not already contain a radical which reacts with ammoniacal silver. (See also § 297.)

439. Aromatic Hydrocarbons and Halides. The nitration test is often serviceable to confirm the presence of an aromatic compound as cited. Care should be taken that this test is not tried in quantity if there is any possibility that the compound is aliphatic, since many of such compounds react violently with nitric acid.

Very cautiously mix a *few drops only* of the unknown substance with a mixture of a few drops of fuming nitric acid and a few drops of concentrated sulfuric acid, holding the mouth of the test-tube away from the face. Heat the mixture gently. If the reaction is not violent, mix 1 or 2 cc. of the unknown substance with 3 cc. of fuming nitric acid and 2 cc. of conc. sulfuric acid. Heat the mixture gently (to about 80°) for about 5 minutes. Pour the reaction mixture into cold water. The appearance of a new solid product, or of a high-boiling, strong-smelling liquid suggestive of nitrobenzene, indicates that an aromatic hydrocarbon was involved. If a solid is obtained, recrystallize it from alcohol and preserve as a possible derivative to be presented to the instructor. In fact this test is more useful for preparation of a derivative than for identification of type.

440. Distinction Between Aliphatic and Aromatic Compounds. The Friedel-Crafts reaction, applicable only to aromatic compounds, often gives striking colorations. The following test is significant if positive, but does not prove absence of aromatic compound if it fails.

Heat about 0.3 g. of anhydrous aluminum chloride in a small dry test tube held nearly horizontally until the material sublimes, and solid has been redeposited 3 or 4 cm. above the bottom of the tube. Now allow the tube to cool slightly, so that the next operation will be less likely to crack the tube. While the tube is still rather hot, introduce about 0.05 g. of a solid unknown substance, or one drop of a liquid, followed by 2 to 3 drops of chloroform. The appearance of a bright coloration, ranging from orange to blue, indicates an aromatic nucleus in the compound tested.

441. Preparation of the Derivative. It is much easier to prepare a small quantity of a solid than of a liquid derivative in a pure state. Moreover, the determination of melting point with very small quantities is easier than the experiment in determination of boiling point. Accordingly the student is urged to make solid derivatives if possible.

The following reactions, or transformations, are often serviceable for preparation of derivatives. The student should improvise shortcut, small-scale directions for preparation, perhaps after first examining standard directions for similar cases in laboratory manuals.

Hydrocarbons and halides, aromatic → nitro, dinitro, and trinitro compounds.

Alcohols, aliphatic → esters of 3,5-dinitrobenzoic acid. (See § 442.)

Phenols → bromo and nitro derivatives.

Acids → *p*-toluidides.

Esters, anhydrides, amides, acyl halides, nitriles, salts → hydrolysis products.

Amines → amides (of simple acids like acetic, benzoic).

Many other derivatives are cited by Kamm and by Shriner and Fuson.

IDENTIFICATION OF AN UNKNOWN ALCOHOL

3,5-Dinitrobenzoic Esters

442. In view of the fact that the esters of 3,5-dinitrobenzoic acid are nearly all crystallizable solids of definite melting point, alcohols may be identified from very small samples by conversion into the esters of this acid. The acid-chloride method of esterification is used, being much more rapid and effective than the simpler acid-alcohol

synthesis earlier described. The melting points of many of these esters are known.

443. Preparation of the Acid Chloride. Mix in a test tube about 0.3 g. of powdered or finely crystalline 3,5-dinitrobenzoic acid with about 0.4 g. of phosphorus pentachloride. (Since both phosphorus pentachloride and phosphorus oxychloride, the by-product of the reaction, are offensive and injurious to the mucous membranes of the eyes and nose, conduct the experiment outdoors or in a hood until you have finished heating the alcohol with the reaction product, as outlined below.)

Warm the mixture of 3,5-dinitrobenzoic acid and phosphorus pentachloride gently over a small flame until the reaction starts. Now remove the tube from the flame. After the reaction subsides, resume the gentle heating and continue until all solid matter has dissolved, so that only a pale-yellow liquid remains. Pour this liquid out upon a watch glass and stir with a glass rod until it becomes a thick paste. Transfer the pasty mass to a small piece of unglazed clay plate. Stir and spread the material until most of the residual liquid has been absorbed by the clay and the solid acid chloride is fairly dry.

444. Preparation of the Ester. Transfer the solid residue of acid chloride from the plate to a dry test tube, and add 0.5 cc. (not more!) of the unknown alcohol. Heat the test tube in a water bath (100°) for 20 minutes; that is, until there has been time for complete esterification. This may require less than 10 minutes for certain simple primary alcohols; but the possible presence of secondary alcohols leads to the requirement for longer time. Tertiary alcohols are not issued in this experiment.

Now add 5 to 10 cc. of water to dissolve a possible residue of acidic by-products. If not already solid, the organic material, or crude ester product, should soon solidify, and may adhere to the test tube. Pass the water solution from the tube through a small filter, and return any solid matter from the filter to the test tube. Crush any large particles with a glass rod, and shake the granular mass of crude ester thoroughly with dilute sodium carbonate solution. Filter the mixture and wash the residue with cold water.

Dissolve the crude ester in the minimum quantity of warm ethyl alcohol. (Do not boil the alcohol, lest the vapors catch fire.) At

least 5 cc. of alcohol will be needed, and in some cases 10 or even 15 cc. Now cool the alcoholic solution to room temperature, whereupon the desired crystals should appear. Sometimes, however, particularly with esters of low melting point, the solution may remain supersaturated in spite of much cooling. In this event add water drop by drop until a precipitate appears. Do not add water after precipitation starts; such addition will cause the separation of an excessive amount of relatively impure product. Crystallization should now proceed in the ordinary way. Now filter the mixture, place the crystals upon a clean piece of porous plate, or even a piece of smooth filter paper, and allow to dry for 24 hours or more.

When the crystals are thoroughly dry, determine the melting point.

MELTING POINTS OF 3,5-DINITROBENZOIC ESTERS

Methyl	107°	n-Nonyl	52°	sec-Butyl	75°
Ethyl	93	n-Decyl	57	Diethyl carbinol	97
n-Propyl	74	iso-Propyl	122	tert-Butyl	142
n-Butyl	64	iso-Butyl	86	tert-Amyl	117
n-Amyl	46	iso-Amyl	62	Allyl	48
n-Hexyl	58	iso-Hexyl	69	sec-Butyl carbinol	62
n-Heptyl	47	iso-Heptyl	54	Cyclohexanol	112
n-Octyl	61	iso-Octyl	58	Benzyl	112

APPENDIX

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APPENDIX

445. Table of Vapor Pressures in Millimeters of Mercury

Temp. Deg. C.	Water	Ethyl Ether	n-Pentane	n-Heptane	n-Octane	Bromo-Benzene	p-Di-bromo-Benzene	a-Bro-monaph-thalene
0°	5	185	183	11	3			
10	9	292	282	21	6			
20	17	442	420	36	10			
30	32	647	611	58	18	6		
40	55	921	873	92	31	10		
50	92	1277	1193	141	49	17		
60	149	1729	1605	209	78	28		
70	233	2296	2119	302	118	44	4	
80	355	2994	2735	427	175	66	7	
90	525	3841	3498	589	253	98	12	
91	546		3580	607	263	102	12	
92	567		3665	625	273	106	13	
93	588		3750	644	283	110	13	
94	611		3838	664	293	114	14	
95	634		3929	684	303	118	15	
96	657		4021	705	313	122	15	
97	682		4114	726	324	127	16	
98	707		4211	748	334	131	17	
99	733		4310	771	344	136	17	
100	760		4410	795	354	141	18	
110	1075			1047	482	199	28	4
120	1489			1367	646	275	42	6
130	2026				859	373	63	9
140	2711				1114	496	89	13
150	3570				1425	649	129	19
160	4636					846	178	27
170	5940					1077	234	39
180	7520					1351	316	55
190	9413					1684	407	75
200	11659						525	102
210	14305						660	134
220	17395							179
230	20978							233
240	25100							300
250	29818							382
260	35188							482
270	41261							604
280	48104							743

446. Boiling Points of Water and Naphthalene at Various Barometric Pressures.

Pressure, mm. Mercury	Boiling Pt. Water	Pressure	B. Pt. of Water	B. Pt. of Naphthalene
610	94.0° C.	720	98.5°	215.7°
620	94.4	725	98.7	216.0
630	94.8	730	98.9	216.3
640	95.3	735	99.1	216.6
650	95.7	740	99.3	216.9
660	96.1	745	99.4	217.2
670	96.5	750	99.6	217.5
680	96.9	755	99.8	217.8
690	97.3	760	100.0	218.1
700	97.7	765	100.2	218.4
710	98.1	770	100.4	218.7

More extended vapor pressure tables for water, and data useful in calculating other vapor pressures for naphthalene, may be found in *Int. Critical Tables*, 3, 212, 226. See also § 445.

447. Common Laboratory Reagents.

Acid, acetic, "glacial"; density 1.05. This is industrially pure acetic acid, containing less than 1% of water.

Acid, hydrochloric, concentrated; density 1.18. An approx. 38% solution of hydrogen chloride in water; concentration about 12N; colorless. The common commercial grade, usually of yellowish tint, is likely to be of slightly lower concentration and density.

Acid, nitric, concentrated; density 1.42. This is the constant-boiling mixture of 68 parts by weight of HNO_3 and 32 parts of water. Approximately 16N.

Acid, nitric, (yellow) fuming; density about 1.5. This is a product which at the time of manufacture was mainly anhydrous nitric acid. By the time it reaches the purchaser it has probably decomposed slightly, and may consist of about 96% HNO_3, the balance being water and oxides of nitrogen. Approx. 24N.

Acid, nitric, (red) fuming; density about 1.54. This is HNO_3 plus a greater excess of oxides of nitrogen.

Acid, sulfuric, concentrated; density about 1.84. Industrially pure H_2SO_4, containing about 6% of water. Approximately 36N.

Acid, sulfuric, fuming; mixtures of H_2SO_4 with varying percent-

ages of SO_3. Should be labeled with a percentage number; for example, "20% fuming" acid is a mixture of 80 parts by weight of H_2SO_4 with 20 parts of SO_3. Often called "oleum."

Ammonium hydroxide, concentrated; density 0.90. A 28% aqueous solution of ammonia, NH_3. Approx. 15N.

448. Melting Points of Mixtures of Acetic Acid with Water

PERCENTAGE OF ACID—DEGREES C.

100%	16.67°	92.6%	6.25°	70%	−18.1°
99	14.80	89.2	2.7	60	−26.6
98	13.25	87	− 0.2	47	−19.3
96.2	10.5	75.4	−12.8	10	− 3.4

449. Saponification Values of Common Fats

Beef tallow	196–200	Linseed oil	188–195
Beeswax	88–96	Mutton tallow	195–196
Butter fat	210–230	Olive oil	185–196
Castor oil	175–183	Peanut oil	186–194
Coconut oil	253–262	Rape seed oil	168–179
Corn oil	187–193	Sesame oil	188–193
Cottonseed oil	194–196	Sperm oil	120–137
Lard	193–203	Wool fat	82–130

Selection of Experiments

The following list of experiments is an example of a program for a one-semester course, 6 hours of laboratory work per week, for students who have had full normal preparation in college inorganic chemistry. In this list it is assumed that the whole field of ordinary organic chemistry, both aliphatic and aromatic, is considered in the one semester in the interests of those students who may not take any further courses in the subject. The assignment is not heavy, thus giving opportunity for the extra attention to principles of manipulation featured in this volume. An allowance of 3 semester hours of credit is desirable.

Calibration of Thermometer
Absolute Alcohol, or Fractional Distillation
Ethyl Iodide or *n*-Butyl Bromide
Propylene and Propylene Dibromide, or Amylene, Acetylene
Diethyl Ether
Acetone or Propionaldehyde
Acetyl Chloride or Acetic Anhydride
Fats and Soaps, Esters of Acetic Acid, or Equivalent Weight of Ester
Acetamide
Carbohydrates (in part)
Melting Point of Unknown Substance, Longer Experiment (delayed in this program so as to give time for the proper preliminary theoretical treatment)
Nitrobenzene or 2,4-Dinitrotoluene
Aniline and Acetanilide
Phenol
Methyl Orange or Phenyl-azo-β-naphthylamine

Supplementary Assignments

Two or more experiments offering choice according to student interests:
Fluorescein and Eosin
Aspirin or Sulfanilamide
Qualitative Organic Analysis of Unknown Substance

The following experiments are suitable for students of limited training and skill. A high percentage of success in making preparations may be expected from this list, and without great expenditure of time.

Recrystallization of a Crude Product
Qualitative Tests for Elements
Melting Point of an Unknown Substance (Shorter Experiment)
tert-Butyl Chloride
Amylene
Acetone and Fractional Distillation
Glacial Acetic Acid
Fats and Soaps, and Esters of Acetic Acid
Hydrolysis of Ethyl Benzoate (as in §§ 260–261)

354

Carbohydrates
Nitrobenzene, and 2,4-Dinitrotoluene
Aniline and Acetanilide
Phenol
Benzyl Alcohol and Benzoic Acid
Methyl Orange

Benzoin and Benzil
Benzoquinone
Cis-Trans Isomerism
Aspirin

A second semester course will usually present many options. Most of the following general suggestions should, however, find place on the program.

A distillation under reduced pressure
Synthesis requiring use of metallic sodium
A Grignard synthesis
A preparation from benzaldehyde
A cyanide reaction; e.g., benzyl cyanide
At least one diazo synthesis
Synthesis requiring condensation at the carbonyl group of aldehyde, ketone or ester

Syntheses illustrating oxidation and reduction of carbon
Preparation of an amino acid
A synthetic sequence
An example from qualitative organic analysis
A short research problem, with term paper

Laboratory Supplies

(a) *Side-Shelf Reagents and Accessories*

Acetic acid, conc. (glacial) and 6N

Hydrochloric acid, conc. and 6N

Nitric acid, conc.

Sulfuric acid, conc.

Ammonia, aqueous, conc. and dilute

Sodium carbonate, dilute (2N)

Sodium hydroxide, 6N

Indicator Solutions: phenolphthalein, methyl orange, methyl violet, Congo Red

Calcium chloride, anhydrous, granular

Carbon, decolorizing (Norite or equivalent)

Cotton and glass wools

Potassium permanganate, cryst.

Salt, common, dairy

Sodium acid sulfite

Sodium dichromate, dihydrate or anhydrous

Stopcock lubricant

Zinc dust

First-Aid Accessories:

Sodium bicarbonate, saturated solution

Boric acid, saturated solution

Sodium thiosulfate, 10% solution

Eye cup

(Also standard first-aid kit)

Solutions Used Occasionally:

Bromine, solution in carbon tetrachloride

Bromine water, saturated

Calcium chloride, saturated

Cleaning solvent, petroleum

Fehling's solutions, Nos. 1 and 2

Schiff's reagent

Silver nitrate, 0.05N

(b) *Special Materials for the Experiments* (*Numbered by Section*)

The following list indicates the quantities to be provided for the performance of each experiment by one student, and is primarily for use of the laboratory buyer. **Caution.** *Students are warned that the quantities specified below are rounded-off values, often somewhat in excess, and are unsuitable for experimental calculations.* Units of measurement are those generally used by American dealers in sales to educational institutions. A generous excess allowance should be provided, especially if the materials are not charged to students by individual items. Side-shelf reagents used in minor quantities are not listed. Materials for which no quantities are specified are used only in very small amounts for test purposes.

356

181. Cleaning Solution
Sodium dichromate	0.01 lb.
Sulfuric acid, conc.	0.4 lb.

182. Magnesium Sulfate
"Bath" Epsom Salt	0.1 lb.

189. Separation and Purification
Methyl alcohol, ethyl alcohol, carbon tetrachloride, toluene, chloroform, benzene, acetone. 0.015 gal. of each as needed.

Sulfanilic acid, tech., gray	10 g.
Acetanilide	5 g.
Benzoic acid	5 g.
Benzil	5 g.
m-Nitroaniline	3 g.
Picric acid	10 g.
Hexachloroethane	2 g.
Anthracene, crude	4 g.

199. Melting Point
Benzoic acid, C.P.	5 mg.
Liquid for bath	150 cc.

211. Molecular Weight
Camphor	3 g.

212. Absolute Alcohol
Quicklime, tech.	0.15 lb.
Alcohol, ethyl 95%	0.04 gal.
Paraffin test oil (See special directions for preparation, p. 363)	0.004 gal.
Dicyclohexyl, optional	15 g.
Cupric sulfate, anhyd.	
Potassium permanganate	

220. Ethyl Iodide
Alcohol, ethyl 95%	0.01 gal.
Phosphorus, red	0.006 lb.
Iodine	0.06 lb.
Calcium chloride	0.005 lb.

222. n-Butyl Bromide
Potassium bromide	0.18 lb.
n-Butyl alcohol	0.013 gal.
Sulfuric acid, conc.	0.4 lb.
Calcium chloride	0.007 lb.

224. tert-Butyl Chloride
tert-Butyl alcohol	25 g.
Hydrochloric acid, conc. C.P.	0.25 lb.
Calcium chloride	0.02 lb.

225. Propylene and Propylene Dibromide
Sulfuric acid, conc.	0.2 lb.
Alcohol, isopropyl	0.02 gal.
Sodium chloride	0.3 lb.
Calcium chloride	0.01 lb.
Bromine	0.7 lb.
Broken clay plate	0.01 lb.

229. Amylene and Acetylene
Sulfuric acid, conc.	0.1 lb.
tert-Amyl alcohol	0.012 gal.
Calcium carbide	0.03 lb.

Cuprous chloride, silver nitrate, bromine water, potass. permanganate.

234. Diethyl Ether
Alcohol, ethyl 95%	0.05 gal.
Sulfuric acid, conc.	0.25 lb.
Calcium chloride	0.025 lb.

236. Propionaldehyde
Sodium dichromate	0.2 lb.
Sulfuric acid, conc.	0.25 lb.
n-Propyl alcohol	50 g.
Magnesium sulfate	0.01 lb.

Silver nitrate and Fehling's solutions.

241. Acetone
Sulfuric acid, conc.	0.2 lb.
Isopropyl alcohol, anhydrous	0.01 gal.
Sodium dichromate	0.12 lb.

245. Haloform Reaction
Hypochlorite solution, household	1.5 fl. oz.
Acetone	0.005 gal.
Bromine	0.03 lb.
Potassium iodide	0.012 lb.

249. Acetic Acid
Sodium acetate, anhyd.	0.1 lb.
Sulfuric acid, conc.	0.1 lb.

251. Acetyl Chloride
Acetic acid, glacial	0.15 lb.
Phosphorus trichloride	0.12 lb.

253. Acetic Anhydride
Sodium acetate, anhyd.	0.25 lb.
Acetyl chloride	0.11 lb.

255. Ethyl Acetate
Alcohol, ethyl 95%	0.02 gal.
Sulfuric acid, conc.	0.06 lb.
Acetic acid, glacial	0.12 lb.
Magnesium sulfate	0.02 lb.

256. Acetate Esters
Supply of propyl, butyl, and amyl alcohols.
Acetic acid, glacial	0.1 lb.
Calcium chloride	0.05 lb.
Magnesium sulfate	0.02 lb.

259. Equivalent of Ester
Alcohol, ethyl 95%	0.04 gal.
Potassium hydroxide	0.01 lb.
Standard sulfuric acid (0.5N)	100 cc.

260. Hydrolysis
Alcohol, ethyl 95%	0.01 gal.
Ester sample	15 g.
Sodium hydroxide	0.03 lb.

263. Fats and Soaps
Fat or oil (see exp.)	0.02 lb.
Potassium hydroxide	0.02 lb.
Alcohol, ethyl 95%	0.02 gal
Trisodium phosphate, dil. soln.	
Sulfate soap.	0.01 lb.

268. Acetamide
Ammonium carbonate	0.15 lb.
Acetic acid, glacial	0.25 lb.
Urea	5 g.
Bromine water.	

273. Reactions of Sugars
Acetic anhydride	7 g.
Acetic acid, glacial	0.05 lb.
Phenylhydrazine hydrochloride	0.4 g.

Chloroform	0.06 lb.
Glucose, sucrose, starch, cotton, sodium acetate, formaldehyde, silver nitrate, Fehling's solutions.	

275. Mucic Acid
Lactic acid	0.02 lb.
Nitric acid, conc.	0.1 lb.

276. β-d-Glucose pentacetate
Glucose	0.012 lb.
Sodium acetate, anhyd.	0.01 lb.
Acetic anhydride	0.07 lb.
Ethyl alcohol	0.01 gal.

277. Inversion of Sucrose
Sugar	0.05 lb.
Phenylhydrazine	2 g.
Hydrochloric acid.	

282. Cellulose Nitrate
Nitric acid, conc.	0.06 lb.
Sulfuric acid, conc.	0.1 lb.
Ether, alcohol, cotton.	

283. Cellulose Acetate
Acetic anhydride	7 g.
Chloroform	0.06 lb.
Cotton.	

285. Nitrobenzene
Sulfuric acid, conc.	0.2 lb.
Nitric acid, conc.	0.15 lb.
Benzene	0.015 gal.
Urea	1 g.
Calcium chloride	0.02 lb.

287. 2,4-Dinitrotoluene
Sulfuric acid, conc.	0.07 lb.
Nitric acid, fuming	0.04 lb.
p-Nitrotoluene	14 g.
Methyl alcohol	0.02 gal.

288. 2,4-Dinitrophenylacetic Acid
Sulfuric acid, conc.	0.2 lb.
Nitric acid, fuming	0.07 lb.
Phenylacetic acid	15 g.

289. p-Nitrobenzoic Acid
p-Nitrotoluene	15 g.

Sodium dichromate	0.12 lb.
Sulfuric acid, conc.	0.3 lb.
Sodium acid sulfite	0.001 lb.
Acetic acid	0.05 lb.

291. Aniline and Acetanilide

Tin, metal, mossy	0.02 lb.
Nitrobenzene	5 g.
Hydrochloric acid, conc.	0.1 lb.
Sodium hydroxide.	
Acetic anhydride	3 g.

297. β-Phenylhydroxylamine

Nitrobenzene	25 g.
Ammonium chloride	0.03 lb.
Zinc dust	0.1 lb.
Salt, common	0.1 lb.

299. Nitrosobenzene

Sulfuric acid, conc.	0.2 lb.
Sodium dichromate	0.03 lb.
Alcohol, ethyl 95%	0.01 gal.

302. Sulfanilic Acid

| Aniline | 0.04 lb. |
| Sulfuric acid, conc. | 0.15 lb. |

303. Sulfonic Acid (Nitro-)

p-Nitrotoluene	20 g.
Sulfuric acid, conc., fuming 20%	0.12 g.
Potassium carbonate	0.25 lb.

305. Bromobenzene

Benzene	0.01 gal.
Bromine	0.2 lb.
Magnesium sulfate	0.02 lb.
Shingle nails.	

309. Phenol

Aniline	0.03 lb.
Sulfuric acid, conc.	0.16 lb.
Urea	2 g.
Sodium nitrite	0.03 lb.
Ether, diethyl	0.3 lb.
or di-isopropyl	0.05 gal.
Magnesium sulfate	0.02 lb.

313. p-Bromotoluene

| p-Toluidine | 45 g. |

Sulfuric acid, conc.	0.3 lb.
Sodium nitrite	0.07 lb.
Cupric sulfate	0.3 lb.
Zinc dust	0.04 lb.
Potassium bromide	0.3 lb.
Magnesium sulfate	0.02 lb.

315. p-Tolylarsonic Acid

Sodium carbonate, anhyd.	0.1 lb.
Arsenious oxide	0.04 lb.
Cupric sulfate	0.003 lb.
Sodium formaldehyde-sulfoxylate	0.01 lb.
p-Toluidine	15 g.
Sodium nitrite	0.025 lb.
Hydrochloric acid, conc.	0.15 lb.

319. p-Nitrosodimethylaniline

Hydrochloric acid, conc.	0.5 lb.
Dimethylaniline	25 g.
Sodium nitrite	0.03 lb.
Benzene	0.04 gal.
Magnesium sulfate	0.02 lb.
Petroleum ether	0.03 gal.

322. Phenyl-azo-β-Naphthylamine

Aniline, pure	3 g.
Sodium nitrite, C.P.	0.01 lb.
β-Naphthylamine, pure	5 g.
Sodium acetate	0.02 lb.
Alcohol, ethyl 95%	0.03 gal.
β-Naphthol	0.1 g.

327. Methyl Orange

Sulfanilic acid, white	10 g.
Sodium nitrite	0.01 lb.
Dimethylaniline	7 g.

330. Phenylhydrazine Hydrochloride

Hydrochloric acid, conc.	0.8 lb.
Aniline	0.05 lb.
Sodium nitrite	0.04 lb.
Sodium hydroxide	0.05 lb.
Sodium acid sulfite	0.15 lb.

335. Benzyl Alcohol and Benzoic Acid

| Benzaldehyde | 40 g. |
| Di-isopropyl ether | 0.04 gal. |

Sodium hydroxide	0.06 lb.
Hydrochloric acid, conc.	0.4 lb.
Sodium acid sulfite	0.01 lb.
Magnesium sulfate	0.02 lb.

337. Benzalacetone
Benzaldehyde	25 g.
Acetone	0.015 gal.
Chloroform	0.06 lb.

339. Benzoin and Benzil
Benzaldehyde	40 g.
Alcohol, ethyl 95%	0.02 gal.
Nitric acid, conc.	0.2 lb.
Sodium cyanide	0.01 lb.

342. Benzilic Acid
Benzil	20 g.
Alcohol, ethyl 95%	0.015 gal.
Potassium hydroxide	0.05 lb.

344. Cinnamic Acid
Benzaldehyde	15 g.
Acetic anhydride	20 g.
Pyridine	0.2 g.
Potassium carbonate	0.02 lb.
Sodium hydroxide	0.03 lb.
Acetic acid, glacial	0.06 lb.
Benzene.	

345. Quinone and Quinhydrone
Hydroquinone	10 g.
Potassium bromate	0.015 lb.

347. Anthraquinone
Anthracene	2 g.
Sodium dichromate	0.015 lb.
Acetic acid, glacial	0.1 lb.

350. n-Octane
n-Butyl bromide	130 g.
Sulfuric acid, conc.	0.4 lb.
Sodium, metallic	0.04 lb.
Magnesium sulfate	0.01 lb.

353. n-Butyl Benzene
n-Butyl bromide	30 g.
Sodium metal	0.03 lb.
Ether	0.05 lb.
Magnesium sulfate, anhyd.	

355. Triphenyl Carbinol
Diethyl ether	0.5 lb
Calcium chloride	0.2 lb.
Phosphorus pentoxide	0.03 lb.
Magnesium turnings	0.01 lb.
Iodine, a crystal.	
Bromobenzene	30 g.
Alcohol, ethyl 95%	0.02 gal.

356. n-Butyl Dimethyl Carbinol
Acetone, n-butyl bromide, quantities
unspecified.

360. Hydrocinnamic Acid
Alcohol, absolute ethyl 99.8%	0.07 gal.
Sodium, metallic	0.03 lb.
Diethyl malonate	85 g.
Benzyl chloride	65 g.
Ether	0.1 lb.
Potassium hydroxide	0.3 lb.
Hydrochloric acid, conc.	0.8 lb.

361. Dry Ethyl Alcohol
Alcohol, ethyl, "absolute"	0.1 gal.
Sodium metallic	0.015 lb.
Ethyl formate	20 cc.

363. Methyl Amyl Ketone
Alcohol, absolute ethyl 99.8%	0.06 gal.
Sodium, metallic	0.02 lb.
Ethyl acetoacetate	48 g.
n-Butyl bromide	55 g.
Sodium hydroxide	0.1 lb.
Calcium chloride	0.1 lb.
Magnesium sulfate	0.02 lb.

365. Diphenylmethane
Benzene, pure	0.04 gal.
Benzyl chloride	40 g.
Aluminum chloride, anhyd.	0.025 lb.

368. α-Bromopropionic Acid
Propionic acid	75 g.
Phosphorus, red	0.003 lb.
Bromine	0.5 lb.

370. Methylmalonic Acid
α-Bromopropionic acid	155 g.

Sodium carbonate 0.15 lb.
Sodium cyanide 0.12 lb.
Sodium hydroxide 0.2 lb.
Sodium sulfate, hydr. 0.4 lb.
Hydrochloric acid, conc. 0.8 lb.
Diethyl ether 1 lb.
Petroleum ether 0.07 gal.
Benzene 0.03 gal.
Magnesium sulfate 0.1 lb.

371. Benzyl Cyanide
Sodium cyanide 0.07 lb.
Alcohol, ethyl 95% 0.015 gal.
Benzyl chloride 65 g.
Magnesium sulfate 0.02 lb.

373. α-Hydroxy α-Methylbutyric Acid
Sodium cyanide 0.2 lb
Methyl ethyl ketone 110 g.
Sodium acid sulfite 0.5 lb.
Hydrochloric acid, conc. 0.5 lb.
Sodium sulfate, anhyd. 0.25 lb.
Magnesium sulfate 0.12 lb.
Benzene 0.02 gal.
Petroleum ether 0.05 gal.

377. Crystal Violet
Dimethylaniline 20 g.
Phosphorus oxychloride 0.02 lb.
Michler's ketone 6 g.

380. Fluorescein-Eosin
Phthalic anhydride 8 g.
Resorcinol 11 g.
Zinc chloride, anhyd. 0.02 lb.
Alcohol, ethyl 95% 0.02 gal.
Bromine 0.06 lb.

386. Phenol Red
Insoluble saccharin 10 g.
Phenol 0.06 lb.
Sulfuric acid, conc. 0.05 lb.
Sodium carbonate 0.1 lb.

388. Propionic acid
1-Nitropropane 45 g.
Sulfuric acid, conc. 0.15 lb.

389. Acetoxime
Acetone 0.01 gal.

390. Methyl nitropropane-diol
Formalin 0.1 lb.
Nitroethane 20 g.

391. Maleic and Fumaric Acids
Maleic anhydride 25 g.
Hydrochloric acid, conc. C.P. 0.1 lb.

394. Decarboxylation
2,4-Dinitrophenylacetic acid 2 g.
Glycerol 0.05 lb.
Methyl alcohol 0.005 gal.

397. Diels-Alder Synthesis
Anthracene, pure 2 g.
Maleic anhydride 6 g.
Benzene 0.02 gal.
Ethyl acetate 0.02 gal.

398. Phenacetin
p-Phenetidine 3 g.
Acetic anhydride 3 g.
Sodium acetate 0.005 lb.

400. Aspirin
Salicylic acid 3 g.
Acetic anhydride 6 g.
Diethyl ether 0.3 lb.
Petroleum ether 0.01 gal.

402. Sulfanilamide
Chlorosulfonic acid 45 g.
Acetanilide 10 g.
Ammonia, conc. 0.1 lb.
Hydrochloric acid, sodium bicarbonate.

406. Glycine
Ammonium carbonate 0.2 lb.
Ammonia, conc. 0.25 lb.
Chloroacetic acid 25 g.
Methanol 0.1 gal.
Cupric carbonate, sodium nitrite, solutions of formaldehyde, methyl red, acetic acid.

412. Hippuric Acid
Glycine 3 g.

Benzoyl chloride   7 g.
(Sodium benzoate- for optional
    method)   5 g.
Congo Red paper.

414. Quinoline
Ferrous sulfate, cryst.   0.03 lb.
Glycerol   0.25 lb.
Aniline   0.07 lb.
Nitrobenzene   25 g.
Sulfuric acid, conc.   0.2 lb.
Sodium hydroxide   0.3 lb.
Sodium nitrite   0.02 lb.

419. Qualitative Tests
Cupric oxide, powd.
Copper wire.
Sodium, metallic.

Ferrous sulfate, solution.
Ferric chloride, solution.
Acetic acid, solution.
Lead acetate, solution.
Silver nitrate, solution.

422. Qualitative Analysis
Anhydrous aluminum chloride.
Chloroform.
Sodium nitrite.
β-Naphthol.
Benzene-sulfonyl chloride.
Sodium, metallic.

444. Unknown Alcohol
3,5-Dinitrobenzoic acid   0.3 g.
Phosphorus pentachloride   0.001 lb.
Alcohol, unknown   1 g.

Preparation of Paraffin Test Oil
for Use in § 215

Prepare the best possible "absolute" alcohol (99.9+ %) by prolonged re-fluxing over quicklime, or by the rapid method of § 361. Preserve a middle fraction of the distillate, and determine its water content from the dicyclohexyl point (§ 216). Commercial dicyclohexyl, m. pt. 3.5° (Cat. No. P 4641 of the Eastman Kodak Company of Rochester, New York) was found for this purpose to be almost exactly equivalent to highly purified preparations of the hydrocarbon obtained by recrystallization with the aid of an ice bath.

Now prepare a mixture of the most highly refined kerosene available and colorless paraffin oil (confectioners' oil, or a light, inexpensive intestinal lubricant) in such ratio that it agrees with the graph of § 215 when tested with the special alcohol just prepared. The procedure is best illustrated by an example, as outlined below.

Dicyclohexyl point of the new alcohol	25.4°
The new alcohol is therefore	99.9%
This percentage calls for an oil mixture which will give (according to § 215) a miscibility temperature of—	25.0°

Oil mixture, first approximation of amounts
"Elaine" kerosene (Standard Oil Co. of Calif.)	7 volumes
"Standard White Oil No. 7" (Standard Oil Co. of Calif.)	1 volume

The 7:1 ratio is now adjusted slightly until the oil gives the 25.0° value above prescribed.

Additional alcohol solutions may now be prepared in whatever range of concentrations is appropriate; 99.8, 99.7, etc. With the aid of these a new graph like that of § 215 may be prepared. If the particular commercial oils above mentioned are used, it is likely that no new graph will be needed; that of § 215 will be approximately valid.

Index